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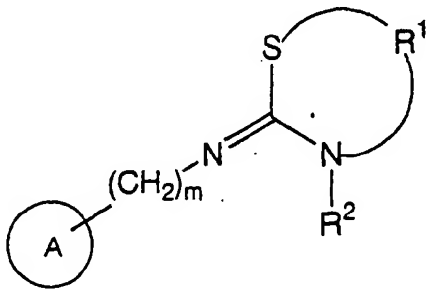
(54) **2-IMINO-1,3-THIAZINE DERIVATIVES**

(57) A compound of the formula (I) of the present invention selectively binds to a cannabinoid type 2 receptor (CB2R) and exhibits an antagonistic activity or agonistic activity to CB2R.



(I)

wherein R^1 is optionally substituted alkylene; R^2 is hydrogen; alkyl; a group of the formula: $-C(=R^5)-R^6$ wherein R^5 is O or S; R^6 is alkyl, alkoxy, alkylthio or the like; or a group of the formula: $-SO_2R^7$ wherein R^7 is alkyl or the like; m is an integer of 1 to 2; A is optionally substituted aromatic carbocycle or the like.

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Description

Technical Field

[0001] The present invention relates to 2-imino-1,3-thiazine derivatives, in detail, 2-imino-1,3-thiazine derivatives having a selective antagonistic activity or agonistic activity to a cannabinoid type 2 receptor and pharmaceutical use of themselves.

Background Art

[0002] Cannabinoid was discovered as the main active substance contained in marijuana in 1960 and found to exhibit an activity to the central nervous system (illusion, euphoria, sensory confusion of time and space) and an activity to the peripheral cell system (immunosuppressive activity, anti-inflammatory activity, analgesic activity).

[0003] After that, anandamide and 2-arachidonoylglycerol produced from phospholipid containing arachidonic acid were discovered as endogenous agonists to a cannabinoid receptor. These endogenous agonists were known to exhibit an activity to the central nervous system and an activity to the peripheral cell system. It was disclosed in Hypertension (1997) 29, 1204-1210 that anandamide exhibits an activity to the cardiovascular system.

[0004] A cannabinoid type 1 receptor discovered in 1990 was found to distribute in the central nervous system such as the brain. Agonists to this receptor were found to suppress the release of neurotransmitters to cause central actions such as illusion or the like. A cannabinoid type 2 receptor discovered in 1993 was found to distribute in immune tissues such as the spleen or the like. Agonists to this receptor were found to suppress an activation of cells in immunocyte or phlogocyte to exhibit an immunosuppressive activity, an anti-inflammatory activity and an analgesic activity (Nature, 1993, 365, 61-65).

[0005] Therefore, selective antagonists or agonists to the cannabinoid type 2 receptor are expected as immunosuppressive agents, anti-inflammatory agents, analgesic agents witout causing side effects on the central nervous system such as illusion or the drug dependence, which are associated with the cannabinoid type 1 receptor (Nature, 1998, 349, 277-281).

[0006] Known as compounds having an antagonistic activity or agonistic activity to the cannabinoid type 2 receptor are isoindolynone derivatives (WO97/29079 and WO99/02499), pyrazole derivatives (WO98/41519) and the like.

[0007] On the other hand, Japanese Patent Publications (Kokai 1986-65894, Kokai 1987-29594) disclose that organophosphorus compounds having a 2-imino-1,3-thiazine skelton are useful as insecticides.

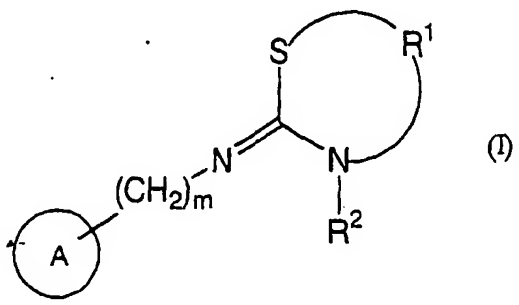
[0008] However, it is not known that 2-imino-1,3-thiazine derivatives have an antagonistic activity or agonistic activity to the cannabinoid type 2 receptor.

Disclosure of Invention

[0009] The present invention provides 2-imino-1,3-thiazine derivatives or the like as novel compounds having a selective antagonistic activity or agonistic activity to the cannabinoid type 2 receptor.

[0010] The present invention comprises,

1) a pharmaceutical composition which comprises a compound of the formula (I):

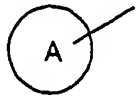


(I)

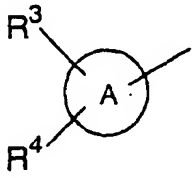
wherein R^1 is optionally substituted alkylene, R^2 is alkyl; a group of the formula: $-C(=R^5)-R^6$ wherein R^5 is O or S, and R^6 is alkyl, alkoxy, alkylthio, optionally substituted amino, optionally substituted aralkyloxy, optionally substituted aralkylthio, optionally substituted aralkylamino, alkoxyalkyl, alkylthioalkyl or optionally substituted aminoalkyl;

or a group of the formula: $-SO_2R^7$ wherein R^7 is alkyl, optionally substituted amino, optionally substituted aryl or optionally substituted heteroaryl, m is an integer of 0 to 2, A is optionally substituted aromatic carbocycle or optionally substituted aromatic heterocycle, a prodrug of itself, a pharmaceutically acceptable salt thereof or a solvate thereof,

2) the pharmaceutical composition according to the above 1) wherein the group of the formula:



is a group of the formula:



wherein R^3 and R^4 each is independently hydrogen, alkyl, alkoxy, alkylthio, optionally substituted amino, optionally substituted aryl, optionally substituted aryloxy, cycloalkyl, halogen, hydroxy, nitro, haloalkyl, haloalkoxy, optionally substituted carbamoyl, carboxy, alkoxycarbonyl, alkylsulfinyl, alkylsulfonyl, alkoxyalkyl, alkylthioalkyl, optionally substituted aminoalkyl, alkoxyalkoxy, alkylthioalkoxy, optionally substituted heteroaryl, optionally substituted non-aromatic heterocyclic gruop, alkoxyiminoalkyl or a group of the formula: $-C(=O)-R^H$ wherein R^H is hydrogen, alkyl, optionally substituted aryl or optionally substituted non-aromatic heterocyclic gruop,
or R^3 and R^4 taken together may form alkylenedioxy, A is optionally substituted aromatic carbocycle or optionally substituted aromatic heterocycle,

3) the pharmaceutical composition according to the above 1) or 2) which has a binding activity to a cannabinoid type 2 receptor,

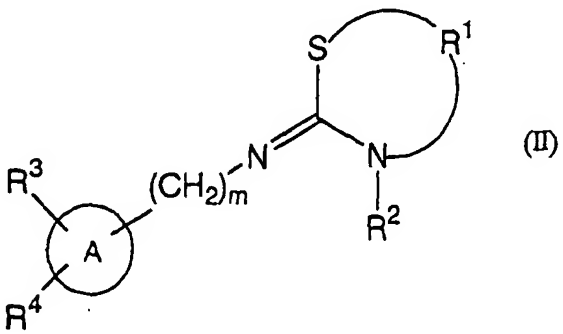
4) the pharmaceutical composition according to the above 3) which has an agonistic activity to a cannabinoid type 2 receptor,

5) the pharmaceutical composition according to the above 3) which is useful as an anti-inflammatory agent,

6) the pharmaceutical composition according to the above 3) which is useful as an immunosuppressive agent,

7) the pharmaceutical composition according to the above 3) which is useful as a nephritis treating agent,

8) a compound of the formula (II):



(II)

wherein R^1 is optionally substituted alkylene, R^2 is a group of the formula: $-C(=R^5)-R^6$ wherein R^5 is O or S, R^6 is alkyl, alkoxy, alkylthio, optionally substituted amino, optionally substituted aralkyloxy, optionally substituted aralkylthio, optionally substituted aralkylamino, alkoxyalkyl, alkylthioalkyl or optionally substituted aminoalkyl, or a group of the formula: $-SO_2R^7$ wherein R^7 is alkyl, optionally substituted amino, optionally substituted aryl or optionally substituted heteroaryl, R^3 and R^4 each is independently hydrogen, alkyl, alkoxy, alkylthio, optionally substituted amino, optionally substituted aryl, optionally substituted aryloxy, cycloalkyl, halogen, hydroxy, nitro,

haloalkyl, haloalkoxy, optionally substituted carbamoyl, carboxy, alkoxycarbonyl, alkylsulfinyl, alkylsulfonyl, alkoxyalkyl, alkylthioalkyl, optionally substituted aminoalkyl, alkoxyalkoxy, alkylthioalkoxy, optionally substituted heteroaryl, optionally substituted non-aromatic heterocyclic group, alkoxyiminoalkyl, or a group of the formula: -C(=O)-R^H wherein R^H is hydrogen, alkyl, optionally substituted aryl or optionally substituted non-aromatic heterocyclic group, or

R^3 and R^4 taken together may form alkylenedioxy, m is an integer of 0 to 2, A is optionally substituted aromatic carbocycle or optionally substituted aromatic heterocycle, a prodrug of itself, a pharmaceutically acceptable salt thereof or a solvate thereof,

9) the compound according to the above 8) wherein m is 0, a prodrug of itself, a pharmaceutically acceptable salt thereof or a solvate thereof,

10) the compound according to the above 8) or 9) wherein R^1 is a C2-C9 straight or branched alkylene optionally substituted with alkylene, a prodrug of itself, a pharmaceutically acceptable salt thereof or a solvate thereof,

11) the compound according to any one of the above 8) to 10) wherein R^1 is a C2-C9 straight alkylene substituted with alkylene, or a C2-C9 branched alkylene, a prodrug of itself, a pharmaceutically acceptable salt thereof or a solvate thereof,

12) the compound according to any one of the above 8) to 11) wherein R^6 is alkoxy or alkylthio, and R^7 is optionally substituted aryl, a prodrug of itself, a pharmaceutically acceptable salt thereof or a solvate thereof,

13) the compound according to any one of the above 8) to 12) wherein R^3 and R^4 each is independently hydrogen, alkyl, alkoxy or alkylthio, and A is optionally substituted aromatic carbocycle, a prodrug of itself, a pharmaceutically acceptable salt thereof or a solvate thereof,

14) the compound according to the above 8) wherein R^1 is 2,2-dimethyltrimethylene, 2,2-diethyltrimethylene, 2,2-ethylenetrimethylene, 1-methyltrimethylene, 2-methyltrimethylene, trimethylene, 2,2-di-n-propyltrimethylene, 2,2-tetramethylenetrimethylene, 2,2-pentamethylenetrimethylene, 1,1-dimethylethylene or 1-methylethylene, R^6 is methyl, ethyl, n-propyl, i-propyl, methoxy, ethoxy, n-propoxy, i-propoxy, n-butoxy, methylthio, ethylthio, n-propylthio, i-propylthio, i-butylthio, sec-butylthio, benzyloxy, benzylthio, methoxymethyl, ethoxymethyl, methylthiomethyl, ethylthiomethyl or ethylamino, R^7 is methyl, ethyl, 4-tolyl, 4-nitrophenyl, 3-nitrophenyl, 2-nitrophenyl, 4-methoxyphenyl, 4-trifluoromethylphenyl, 2-thienyl or 2-naphthyl, R^3 is hydrogen, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, sec-butyl, t-butyl, methoxy, ethoxy, n-propoxy, i-propoxy, n-butoxy, methylthio, ethylthio, n-propylthio, i-propylthio, dimethylamino, acetylamino, N-acetylmethylamino, diethylamino, ethylmethylamino, propylmethylamino, phenyl, phenoxy, fluoro, chloro, bromo, nitro, trifluoromethyl, difluoromethoxy, trifluoromethoxy, N-methylcarbamoyl, methoxycarbonyl, methanesulfinyl, ethanesulfinyl, methanesulfonyl, ethanesulfonyl, acetyl, methoxymethyl, 1-methoxyethyl, 3-pyridyl, morpholino, pyrrolidino, piperidino, 2-oxopyrrolidino, 1-methoxyiminoethyl or morpholinocarbonyl, R^4 is hydrogen, methyl, ethyl, fluoro, chloro, nitro, methoxy or ethoxy, or

R^3 and R^4 taken together may form -O-CH_2-O-, A is benzene, naphthalene, pyridine or quinoline, a prodrug of itself, a pharmaceutically acceptable salt thereof or a solvate thereof,

15) a pharmaceutical composition which comprises the compound according to any one of the above 8) to 14), a prodrug of itself, a pharmaceutically acceptable salt thereof or a solvate thereof,

16) the pharmaceutical composition according to the above 15) which has a binding activity to a cannabinoid type 2 receptor,

17) the pharmaceutical composition according to the above 16) which has an agonistic activity to a cannabinoid type 2 receptor,

18) the pharmaceutical composition according to the above 16) which is useful as an anti-inflammatory agent,

19) the pharmaceutical composition according to the above 16) which is useful as an immunosuppressive agent,

20) the pharmaceutical composition according to the above 16). which is useful as a nephritis treating agent,

21) a method for treating inflammation which comprises administering the pharmaceutical composition according to the above 1),

22) a method of immunosuppression which comprises administering the pharmaceutical composition according to the above 1),

23) a method for treating nephritis which comprises administering the pharmaceutical composition according to the above 1),

24) use of the compound according to the above 1) for manufacturing an anti-inflammatory agent,

25) use of the compound according to the above 1) for manufacturing an immunosuppressive agent, and

26) use of the compound according to the above 1) for manufacturing a nephritis treating agent.

Best Mode for Carrying Out the Invention

[0011] The meanings of each term used in compound of the formula (I) and (II) are explained below. Each term is used to express the same meaning in the specification.

[0012] The term "alkylene" includes a C2-C10 straight or branched alkylene, for example, ethylene, 1-methylethylene, 1-ethylethylene, 1,1-dimethylethylene, 1,2-dimethylethylene, 1,1-diethylethylene, 1,2-diethylethylene, 1-ethyl-2-methylethylene, trimethylene, 1-methyltrimethylene, 2-methyltrimethylene, 1,1-dimethyltrimethylene, 1,2-dimethyltrimethylene, 2,2-dimethyltrimethylene, 1-ethyltrimethylene, 2-ethyltrimethylene, 1,1-diethyltrimethylene, 1,2-diethyltrimethylene, 2,2-diethyltrimethylene, 2-ethyl-2-methyltrimethylene, tetramethylene, 1-methyltetramethylene, 2-methyltetramethylene, 1,1-dimethyltetramethylene, 1,2-dimethyltetramethylene, 2,2-dimethyltetramethylene, 2,2-di-n-propyltrimethylene or the like. Preferred is a C2-C9 straight or branched alkylene. More preferred is a C2-C9 branched alkylene, for example, 2,2-dimethyltrimethylene, 2,2-diethyltrimethylene, 1-methyltrimethylene, 2-methyltrimethylene, trimethylene, 2,2-di-n-propyltrimethylene, 1,1-dimethylethy-lene or 1-methylethylene. The position number of these substituents is based on either the order of N-R^1-S or that of S-R^1-N.

[0013] Examples of substituents of "optionally substituted alkylene" include alkylene (e.g., methylene, ethylene, trimethylene, tetramethylene, pentamethylene or the like), cycloalkyl (e.g., cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl or the like), alkoxy (e.g., methoxy, ethoxy or the like), alkylthio (e.g., methylthio, ethylthio or the like), alkylamino (e.g., methylamino, ethylamino, dimethylamino or the like), acylamino (e.g., acetylamino or the like), aryl (e.g., phenyl or the like), aryloxy(e.g., phenoxy or the like), halogen (fluoro, chloro, bromo, iodo), hydroxy, amino, nitro, alkylsulfonyl (e.g., methanesulfonyl, ethanesulfonyl or the like), arylsulfonyl (e.g., benzenesulfonyl or the like), cyano, hydroxyamino, carboxy, alkoxycarbonyl (e.g., methoxycarbonyl, ethoxycarbonyl or the like), acyl (e.g., acetyl, benzoyl or the like), aralkyl (e.g., benzyl or the like), mercapto, hydorazino, amidino, guanidino or the like. One to four of these substituents may substitute at any position. Preferred as the substituent of "optionally substituted alkylene" is alkylene.

[0014] Alkylene substituted with alkylene include alkylene substituted via a spiro atom with alkylene (e.g., 2,2-ethylenetrimethylene, 2,2-trimethylenetrimethylene, 2,2-tetramethylenetrimethylene, 2,2-pentamethylenetrimethylene or the like) and alkylene substituted at the different positions with alkylene (e.g., 1,2-tetramethyleneethylene, 1,2-ethylenetrimethylene or the like). Preferred examples include 2,2-ethylenetrimethylene, 2,2-trimethylenetrimethylene, 2,2-tetramethylenetrimethylene, 2,2-pentamethylenetrimethylene, especially, 2,2-ethylenetrimethylene, 2,2-tetramethylenetrimethylene and 2,2-pentamethylenetrimethylene.

[0015] The term "alkyl" includes a C1-C10 straight or branched alkyl, for example, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, sec-butyl, tert-butyl, n-pentyl, i-pentyl, neo-pentyl, n-hexyl, n-heptyl, n-octyl, n-noyl, n-decyl or the like. Preferred is a C1-C4 straight or branched alkyl, for example, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, sec-butyl and tert-butyl.

[0016] The term "alkoxy" includes an oxygen atom substituted with the above "alkyl", for example, methoxy, ethoxy, n-propoxy, i-propoxy, n-butoxy, i-butoxy, sec-butoxy, tert-butoxy, n-pentyloxy, n-hexyloxy, n-heptyloxy, n-octyloxy or the like. Preferred is a C1-C4 straight or branched alkoxy, for example, methoxy, ethoxy, n-propoxy, i-propoxy, n-butoxy, i-butoxy, sec-butoxy and tert-butoxy.

[0017] The term "alkylthio" includes a sulfur atom substituted with the above "alkyl", for example, methylthio, ethylthio, n-propylthio, i-propylthio, n-butylthio, i-butylthio, sec-butylthio, tert-butylthio, n-pentylthio, n-hexylthio or the like. Preferred is a C1-C4 straight or branched alkylthio, for example, methylthio, ethylthio, n-propylthio, i-propylthio, n-butylthio, i-butylthio, sec-butylthio and tert-butylthio.

[0018] Examples of substituents of "optionally substituted amino" includes alkyl (e.g., methyl, ethyl, n-propyl, i-propyl or the like), acyl (e.g., formyl, acetyl, propionyl, benzoyl or the like) or the like. A nitrogen atom of an amino group may be mono- or di-substituted with these substituents.

[0019] Examples of "optionally substituted amino" include amino, methylamino, ethylamino, n-propylamino, i-propylamino, dimethylamino, diethylamino, ethylmethylamino, acetylamino, N-acetylmethylamino, propylmethylamino or the like.

[0020] The term "aryl" includes a C6-C14 aromatic carbocyclic group, for example, phenyl, naphthyl, anthryl, phenanthryl or the like.

[0021] The term "aralkyl" includes the above "alkyl" substituted with the above "aryl", for example, benzyl, phenylethyl (e.g., 1-phenylethyl, 2-phenylethyl), phenylpropyl (e.g., 1-phenylpropyl, 2-phenylpropyl, 3-phenylpropyl or the like), naphthylmethyl (e.g., 1-naphthylmethyl, 2-naphthylmethyl or the like) or the like.

[0022] The term "aralkyloxy" includes an oxygen atom substituted with the above "aralkyl", for example, benzyloxy, phenylethyloxy (e.g., 1-phenylethyloxy, 2-phenylethyloxy), phenylpropoxy (e.g., 1-phenylpropyloxy, 2-phenylpropyloxy, 3-phenylpropyloxy or the like), naphthylmethoxy (e.g., 1-naphthylmethoxy, 2-naphthylmethoxy or the like) or the like.

[0023] The term "aralkylthio" includes a sulfur atom substituted with the above "aralkyl", for example, benzylthio, phenylethylthio (e.g., 1-phenylethylthio, 2-phenylethylthio), phenylpropylthio (e.g., 1-phenylpropylthio, 2-phenylpropylthio, 3-phenylpropylthio or the like), naphthylmethylthio (e.g., 1-naphthylmethylthio, 2-naphthylmethylthio or the like) or the like.

[0024] The term "aralkylamino" includes a nitrogen atom substituted with one or two of the above "aralkyl", for example, benzylamino, phenylethylamino (e.g., 1-phenylethylamino, 2-phenylethylamino), phenylpropylamino (e.g., 1-phenylpropylamino, 2-phenylpropylamino, 3-phenylpropylamino), naphthylmethylamino (e.g., 1-naphthylmethylami-

no, 2-naphthylmethylamino or the like), dibenzylamino or the like.

[0025] The term "alkoxyalkyl" includes the above "alkyl" substituted with the above "alkoxy", for example, methoxymethyl, ethoxymethyl, n-propoxymethyl, 1-methoxyethyl, 2-methoxyethyl, 1-ethoxyethyl, 2-ethoxyethyl, 1-n-propoxyethyl, 2-n-propoxyethyl, 1-methoxy-n-propyl, 2-methoxy-n-propyl, 3-methoxy-n-propyl, 1-ethoxy-n-propyl, 2-ethoxy-n-propyl, 3-ethoxy-n-propyl, 1-n-propoxy-n-propyl, 2-n-propoxy-n-propyl, 3-n-propoxy-n-propyl or the like.

[0026] The term "alkylthioalkyl" includes the above "alkyl" substituted with the above "alkylthio", for example, methylthiomethyl, ethylthiomethyl, n-propylthiomethyl, 1-methylthioethyl, 2-methylthioethyl, 1-ethylthioethyl, 2-ethylthioethyl, 1-n-propylthioethyl, 2-n-propylthioethyl, 3-n-propylthioethyl, 1-methylthio-n-propyl, 2-methylthio-n-propyl, 3-methylthio-n-propyl, 1-ethylthio-n-propyl, 2-ethylthio-n-propyl, 3-ethylthio-n-propyl, 1-n-propylthio-n-propyl, 2-n-propylthio-n-propyl, 3-n-propylthio-n-propyl or the like.

[0027] The term "optionally substituted aminoalkyl" includes the above "alkyl" substituted with the above "optionally substituted amino", for example, N-methylaminomethyl, N-acetylaminomethyl, N,N-dimethylaminomethyl or the like.

[0028] The term "alkoxyalkoxy" includes the above "alkoxy" substituted with the above "alkoxy", for example, methoxymethoxy, ethoxymethoxy, n-propoxymethoxy, isopropoxymethoxy, 1-methoxyethoxy, 2-methoxyethoxy or the like.

[0029] The term "alkylthioalkoxy" includes the above "alkoxy" substituted with the above "alkylthio", for example, methylthiomethoxy, ethylthiomethoxy, n-propylthiomethoxy, isopropylthiomethoxy, 1-methylthioethoxy, 2-methoxyethoxy or the like.

[0030] The term "heteroaryl" includes a C1-C9 heteroaryl having one to four nitrogen atom(s), oxygen atom(s) and/or sulfur atom(s), for example, furyl (e.g., 2-furyl, 3-furyl), thienyl (e.g., 2-thienyl, 3-thienyl), pyrrolyl (e.g., 1-pyrrolyl, 2-pyrrolyl, 3-pyrrolyl), imidazolyl (e.g., 1-imidazolyl, 2-imidazolyl, 4-imidazolyl), pyrazolyl (e.g., 1-pyrazolyl, 3-pyrazolyl, 4-pyrazolyl), triazolyl (e.g., 1,2,4-triazol-1-yl, 1,2,4-triazol-3-yl, 1,2,4-triazol-4-yl), tetrazolyl (e.g., 1-tetrazolyl, 2-tetrazolyl, 5-tetrazolyl), oxazolyl (e.g., 2-oxazolyl, 4-oxazolyl, 5-oxazolyl), isoxazolyl (e.g., 3-isoxazolyl, 4-isoxazolyl, 5-isoxazolyl), thiazolyl (e.g., 2-thiazolyl, 4-thiazolyl, 5-thiazolyl), thiadiazolyl, isothiazolyl (e.g., 3-isothiazolyl, 4-isothiazolyl, 5-isothiazolyl), pyridyl (e.g., 2-pyridyl, 3-pyridyl, 4-pyridyl), pyridazinyl (e.g., 3-pyridazinyl, 4-pyridazinyl), pyrimidinyl (e.g., 2-pyrimidinyl, 4-pyrimidinyl, 5-pyrimidinyl), furazanyl (e.g., 3-furazanyl), pyrazinyl (e.g., 2-pyrazinyl), oxadiazolyl (e.g., 1,3,4-oxadiazol-2-yl), benzofuryl (e.g., 2-benzo[b]furyl, 3-benzo[b]furyl, 4-benzo[b]furyl, 5-benzo[b]furyl, 6-benzo[b]furyl, 7-benzo[b]furyl), benzothienyl (e.g., 2-benzo[b]thienyl, 3-benzo[b]thienyl, 4-benzo[b]thienyl, 5-benzo[b]thienyl, 6-benzo[b]thienyl, 7-benzo[b]thienyl), benzimidazolyl (e.g., 1-benzimidazolyl, 2-benzimidazolyl, 4-benzimidazolyl, 5-benzimidazolyl), dibenzofuryl, benzoxazolyl, quinoxalinyl (e.g., 2-quinoxalinyl, 5-quinoxalinyl, 6-quinoxalinyl), cinnolinyl (e.g., 3-cinnolinyl, 4-cinnolinyl, 5-cinnolinyl, 6-cinnolinyl, 7-cinnolinyl, 8-cinnolinyl), quinazolinyl (e.g., 2-quinazolinyl, 4-quinazolinyl, 5-quinazolinyl, 6-quinazolinyl, 7-quinazolinyl, 8-quinazolinyl), quinolyl (e.g., 2-quinolyl, 3-quinolyl, 4-quinolyl, 5-quinolyl, 6-quinolyl, 7-quinolyl, 8-quinolyl), phthalazinyl (e.g., 1-phthalazinyl, 5-phthalazinyl, 6-phthalazinyl), isoquinolyl (e.g., 1-isoquinolyl, 3-isoquinolyl, 4-isoquinolyl, 5-isoquinolyl, 6-isoquinolyl, 7-isoquinolyl, 8-isoquinolyl), puryl, pteridinyl (e.g., 2-pteridinyl, 4-pteridinyl, 6-pteridinyl, 7-pteridinyl), carbazolyl, phenanthridinyl, acridinyl (e.g., 1-acridinyl, 2-acridinyl, 3-acridinyl, 4-acridinyl, 9-acridinyl), indolyl (e.g., 1-indolyl, 2-indolyl, 3-indolyl, 4-indolyl, 5-indolyl, 6-indolyl, 7-indolyl), isoindolyl, phenazinyl (e.g., 1-phenazinyl, 2-phenazinyl) or phenothiadinyl (e.g., 1-phenothiadinyl, 2-phenothiadinyl, 3-phenothiadinyl, 4-phenothiadinyl) or the like.

[0031] Preferred as heteroaryl of R^3 and R^4 is 3-pyridyl. Preferred as heteroaryl of R^7 is 2-thienyl.

[0032] The ring A includes "optionally substituted aromatic carbocycle" or "optionally substituted aromatic heterocycle".

[0033] The term "aromatic carbocycle" includes a C6-C14 aromatic carbocycle, for example, benzene, naphthalene, anthracene, phenanthrene or the like. Preferred is benzene or naphthalene.

[0034] The term "aromatic heterocycle" includes a C1-C9 aromatic ring having one to four nitrogen atom(s), oxygen atom(s) and/or sulfur atom(s), for example, furan, thiophene, pyrrole, imidazole, pyrazole, triazole, tetrazole, oxazole, isoxazole, thiazole, thiadiazole, isothiazole, pyridine, pyridazine, pyrimidine, furazan, pyrazine, benzofuran, benzothiophene, benzimidazole, dibenzofuran, benzoxazole, quinoxaline, cinnoline, quinazoline, quinoline, phthalazine, isoquinoline, purine, pteridine, carbazole, phenanthridine, acridine, indole, isoindole or phenazine or the like. Preferred is pyridine, quinoline or isoquinoline.

[0035] Examples of the substituents of "optionally substituted aralkyloxy", "optionally substituted aralkylthio", "optionally substituted aralkylamino", "optionally substituted aryl", "optionally substituted heteroaryl", "optionally substituted aryloxy", "optionally substituted aromatic carbocycle", "optionally substituted aromatic heterocycle" and "optionally substituted non-aromatic heterocyclic group" include alkyl, alkoxy, alkylthio, optionally substituted amino, optionally substituted aryl, optionally substituted aryloxy, cycloalkyl, halogen, hydroxy, nitro, haloalkyl, haloalkoxy, optionally substituted carbamoyl, carboxy, alkoxycarbonyl, alkylsulfinyl, alkylsulfonyl, alkoxyalkyl, alkylthioalkyl, optionally substituted aminoalkyl, alkoxyalkoxy, alkylthioalkoxy, optionally substituted heteroaryl, optionally substituted non-aromatic heterocyclic group, alkoxyiminoalkyl, a group of the formula: $-C(=O)-R^H$ wherein R^H is hydrogen, alkyl, optionally substituted aryl or optionally substituted non-aromatic heterocyclic group, arylsulfonyl (e.g., benzenesulfonyl or the like), cyano, hydroxy amino, aralkyl (e.g., benzyl or the like), mercapto, hydrazino, amidino, guanidino, isocyano, isocyanato, thio-

cyanato, isothiocyanato, sulfamoyl, formyloxy, haloformyl, oxalo, thioformyl, thiocarboxy, dithiocarboxy, thiocarbamoyl, sulfino, sulfo, sulfoamino, azido, ureido, amidino, guanidino, oxo, thioxo or the like.

[0036] These substituents may substitute at any substitutable positions. Alkylenedioxy may substitute at the same or different positions on the ring. An example of alkylenedioxy includes -O-CH_2-O-, -O-CH_2-CH_2-O-, -O-CH_2-CH_2-CH_2-O-.

[0037] The term "aryloxy" includes an oxygen atom substituted with the above "aryl", for example, phenoxy, naphthoxy (e.g., 1-naphthoxy, 2-naphthoxy or the like), anthryloxy (e.g., 1-anthryloxy, 2-anthryloxy or the like), phenanthryl (e.g., 1-phenanthryl, 2-phenanthryl or the like) or the like.

[0038] The term "cycloalkyl" includes C3-C7 cycloalkyl, for example, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl or the like.

[0039] The term "halogen" includes fluoro, chloro, bromo and iodo. Preferred is fluoro, chloro or bromo.

[0040] The term "haloalkyl" includes the above "alkyl" substituted with one or more halogen, for example, chloromethyl, dichloromethyl, difluoromethyl, trifluoromethyl, chloroethyl (e.g., 1-chloroethyl, 2-chloroethyl or the like), dichloroethyl (e.g., 1,1-dichloroethyl, 1,2-dichloroethyl, 2,2-dichloroethyl or the like) or the like.

[0041] The term "haloalkoxy" includes the above "alkoxy" substituted with one or more halogen, for example, dichloromethoxy, difluoromethoxy, trifluoromethoxy, trifluoroethoxy (2,2,2-trifluoroethoxy or the like) or the like.

[0042] Examples of the substituents of "optionally substituted carbamoyl" include alkyl (e.g., methyl, ethyl, n-propyl, i-propyl or the like), acyl (e.g., formyl, acetyl, propionyl, benzoyl or the like) or the like. The nitrogen atom of carbamoyl group may be mono- or di-substituted with these substituents.

[0043] Preferred as "optionally substituted carbamoyl" is carbamoyl, N-methylcarbamoyl or N-ethylcarbamoyl.

[0044] The term "alkoxycarbonyl" includes carbonyl substituted with "alkoxy". Preferred is methoxycarbonyl, ethoxycarbonyl or the like.

[0045] The term "alkylsulfinyl" includes sulfinyl substituted with the above "alkyl". Preferred is methanesulfinyl, ethanesulfinyl or the like.

[0046] The term "alkylsulfonyl" includes sulfonyl substituted with the above "alkyl". Preferred is methanesulfonyl, ethanesulfonyl or the like.

[0047] The term "non-aromatic heterocyclic group" includes a C1-C9 non-aromatic ring having one to four nitrogen atom(s), oxygen atom(s) and/or sulfur atom(s), for example, 1-pyrrolinyl, 2-pyrrolinyl, 3-pyrrolinyl, pyrrolidino, 2-pyrrolidinyl, 3-pyrrolidinyl, 1-imidazolinyl, 2-imidazolinyl, 4-imidazolinyl, 1-imiaazolidinyl, 2-imidazolidinyl, 4-imidazolidinyl, 1-pyrazolinyl, 3-pyrazolinyl, 4-pyrazolinyl, 1-pyrazolidinyl, 3-pyrazolidinyl, 4-pyrazolidinyl, piperidino, 2-piperidyl, 3-piperidyl, 4-piperidyl, piperazino, 2-piperazinyl, 2-morpholinyl, 3-morpholinyl, morpholino, tetrahydropyranyl or the like. Preferred is morpholino, pyrrolidino, piperidino or piperazino.

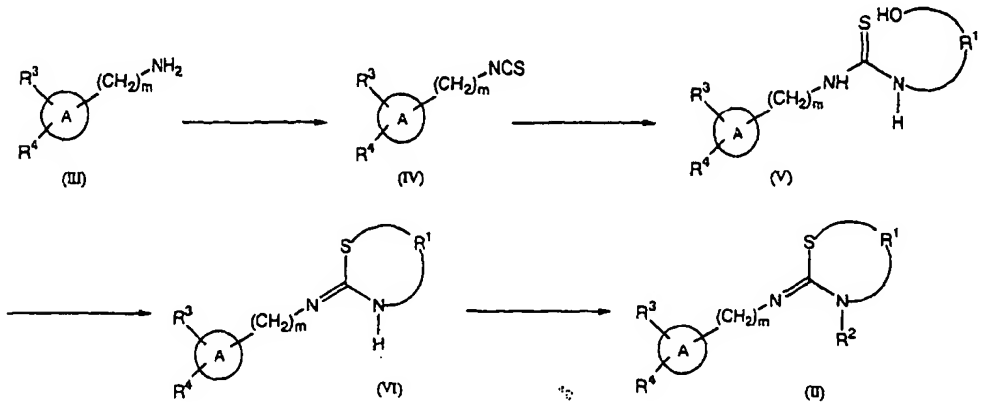
[0048] The term "alkoxyiminoalkyl" include the above "alkyl" substituted with alkoxyimino, for example, methoxyiminomethyl, ethoxyiminomethyl, 1-methoxyiminoethyl or the like.

[0049] Examples of a group of the formula: -C(=O)-R^H wherein R^H is hydrogen, alkyl, optionally substituted aryl or optionally substituted non-aromatic heterocyclic group include formyl, acetyl, benzoyl, toluoyl, morpholinocarbonyl or the like.

[0050] The tem "m" is an integer of 0 to 2. Preferred as "m" is 0.

[0051] The term "an agonistic activity to a cannabinoid type 2 receptor" includes agonizing a cannabinoid type 2 receptor.

[0052] The compounds of the present invention can be prepared in accordance with the following processes.



wherein R^1 is optionally substituted alkylene, R^2 is alkyl; a group of the formula: $-C(=R^5)-R^6$ wherein R^5 is O or S, R^6 is alkyl, alkoxy, alkylthio, optionally substituted amino, optionally substituted aralkyloxy, optionally substituted aralkylthio, optionally substituted aralkylamino, alkoxyalkyl, alkylthioalkyl or optionally substituted aminoalkyl; or a group of the formula: $-SO_2R^7$ wherein R^7 is alkyl, optionally substituted amino, optionally substituted aryl or optionally substituted heteroaryl, R^3 and R^4 each is independently hydrogen, alkyl, alkoxy, alkylthio, optionally substituted amino, optionally substituted aryl, optionally substituted aryloxy, cycloalkyl, halogen, hydroxy, nitro, haloalkyl, haloalkoxy, optionally substituted carbamoyl, carboxy, alkoxycarbonyl, alkylsulfinyl, alkylsulfonyl, alkoxyalkyl, alkylthioalkyl, optionally substituted aminoalkyl, alkoxyalkoxy, alkylthioalkoxy, optionally substituted heteroaryl, optionally substituted non-aromatic heterocyclic group, alkoxyiminoalkyl, or a group of the formula: $-C(=O)-R^H$ wherein R^H is hydrogen, alkyl, optionally substituted aryl or optionally substituted non-aromatic heterocyclic group, or
R^3 and R^4 taken together may form $-O-CH_2-O-$, m is an integer of 0 to 2, A is optionally substituted aromatic carbocycle or optionally substituted aromatic heterocycle.

Process 1

[0053] This is a process for producing a compound of the formula (IV) which comprises converting amino group of a compound of the formula (III) to isothiocyanic acid ester (isothiocyanate).

[0054] A method for converting amino group to isothio cyanic acid ester (isothiocyanate) includes the following methods; 1) a method which comprises reacting the starting compound with carbon disulfide in the presence of a base such as ammonia (NH_3, NH_4OH), triethylamine (Et_3N) and reacting the obtained dithiocarbamate with ethyl chlorocarboxylate ($ClCO_2Et$) and triethylamine (Et_3N), 2) a method which comprises reacting the above dithiocarbamate with acid metalate such as lead nitrate or the like, 3) a method of reacting thiophosgene ($CSCl_2$) and 4) a method of reacting thiocarbonyldiimidazole or the like.

[0055] In the above 1), a base (1.0 to 1.5 mole equivalent) and carbon disulfide (1.0 to 1.5 mole equivalent) are added to a solution of a compound of the formula (III) in an aprotic solvent (e.g., diethylether, tetrahydrofuran, dimethylformamide, benzene, toluene, dichloromethane, chloroform or the like) and the mixture is stirred for 0.5 to 10 hours. After that, ethyl chlorocarboxylate (1.0 to 1.5 mole equivalent) and triethylamine (1.0 to 1.5 mole equivalent) are added thereto and the mixture is stirred in the same solvent for 0.5 to 10 hours. The reaction temperature is preferably 0 to 100 °C, especially 0 °C to room temperature.

[0056] In the above 3), thiophosgene (1.0 to 1.5 mole equivalent) is added to a solution of the compound of the formula (III) in an aprotic solvent (e.g., diethylether, tetrahydrofuran, dimethylformamide, benzene, toluene, dichloromethane, chloroform or the like) and stirred for 0.5 to 10 hours. The reaction temperature is preferably 0 to 100 °C, especially 0 °C to room temperature.

[0057] In the above 4), thiocarbonyldiimidazole (1.0 to 1.5 mole equivalent) is added to a solution of the compound of the formula (III) in an aprotic solvent (e.g., diethylether, tetrahydrofuran, dimethylformamide, benzene, toluene, dichloromethane, chloroform or the like) and stirred for 0.5 to 10 hours. The reaction temperature is preferably 0 to 100 °C, especially 0 °C to room temperature.

[0058] Examples of the compound of the formula (III) wherein m is 0 include aniline, 2-methylaniline, 2-ethylaniline, 2-n-propylaniline, 2-i-propylaniline, 2-n-butylaniline, 2-sec-butylaniline, 2-t-butylaniline, 3-methylaniline, 3-i-propylaniline, 3-i-propyl-4-methylaniline, 3-t-butylaniline, 4-methylaniline, 4-i-propylaniline, 2,6-dimethylaniline, 2,3-dimethylaniline, 2,4-dimethylaniline, 3,4-diethylaniline, 2,5-dimethylaniline, 3,4-dimethylaniline, 3,5-dimethylaniline, 2,6-diethylaniline, 2,6-di-i-propylaniline, 2-methoxyaniline, 2-ethoxyaniline, 2-i-propoxyaniline, 3-methoxyaniline, 3,5-dimethoxyaniline, 3-n-butoxyaniline, 4-n-butoxyaniline, 4-ethoxyaniline, 3,4-dimethoxyaniline, 2-methylthioaniline, 2-ethylthioaniline, 2-i-propylthioaniline, 2-N,N-dimethylaminoaniline, 2-phenylaniline, 3-phenylaniline, 4-phenoxyaniline, 2-cyclohexylaniline, 2-cyclopentylaniline, 2-nitroaniline, 2,4-dinitroaniline, 2-fluoroaniline, 2-chloroaniline, 4-chloroaniline, 2,3-dichloroaniline, 3,4-dichloroaniline, 2-i-propyl-4-nitroaniline, 2-i-propyl-6-nitroaniline, 2-hydroxyaniline, 2-N,N-dimethylaminocarbonylaniline, 2-N-acetylaniline, 2-(1-ethylpropyl)aniline, 2-i-propyl4-methylaniline, 2-i-propyl-4-hydroxyaniline, 2-i-propyl-4-chloroaniline, 2-i-propyl-4-aminoaniline, 2-i-propyl-5-methylaniline, 2-i-propyl-5-hydroxy aniline, 2-i-propyl-5-chloroaniline, 4-chloro-3-methylaniline, 3,4-methylenedioxyaniline or the like.

[0059] Examples of the compound of the formula (III) wherein m is 1 include benzylamine, 2-methylbenzylamine, 2-ethylbenzylamine, 2-n-propylbenzylamine, 2-i-propylbenzylamine, 2-n-butylbenzylamine, 2-sec-butylbenzylamine, 2-t-butylbenzylamine, 3-methylbenzylamine, 3-i-propylbenzylamine, 3-i-propyl-4-methylbenzylamine, 3-t-butylbenzylamine, 4-methylbenzylamine, 4-i-propylbenzylamine, 2,6-dimethylbenzylamine, 2,3-dimethylbenzylamine, 2,4-dimethylbenzylamine, 3,4-diethylbenzylamine, 2,5-dimethylbenzylamine, 3,4-dimethylbenzylamine, 3,5-dimethylbenzylamine, 2,6-diethylbenzylamine, 2,6-di-i-propylbenzylamine, 2-methoxybenzylamine, 2-ethoxybenzylamine, 2-i-propoxybenzylamine, 3-methoxybenzylamine, 3,5-dimethoxybenzylamine, 3-n-butoxybenzylamine, 4-n-butoxybenzylamine, 4-ethoxybenzylamine, 3,4-dimethoxybenzylamine, 2-methylthiobenzylamine, 2-ethylthiobenzylamine, 2-i-propylthiobenzylamine, 2-N,N-dimethylaminobenzylamine, 2-phenylbenzylamine, 3-phenylbenzylamine, 4-phenoxy-

benzylamine, 2-cyclohexylbenzylamine, 2-cyclopentylbenzylamine, 2-nitrobenzylamine, 2,4-dinitrobenzylamine, 2-fluorobenzylamine, 2-chlorobenzylamine, 4-chlorobenzylamine, 2,3-dichiorobenzylamine, 3,4-dichlorobenzylamine, 2-i-propyl-4-nitrobenzylamine, 2-i-propyl-6-nitrobenzylamine, 2-hydroxybenzylamine, 2-N,N-dimethylaminocarbonylbenzylamine, 2-N-acetylbenzylamine, 2-(1-ethylpropyl)benzylamine, 2-i-propyl4-methylbenzylamine, 2-i-propyl-4-hydroxybenzylamine, 2-i-propyl-4-chlorobenzylamine, 2-i-propyl-4-aminobenzylamine, 2-i-propyl-5-methylbenzylamine, 2-i-propyl-5-hydroxybenzylamine, 2-i-propyl-5-chlorobenzylamine, 4-chloro-3-methylbenzylamine, 3,4-methylenedioxybenzylamine or the like.

[0060] Examples of the compound of the formula (III) wherein m is 2 include phenethylamine, 2-methylphenethylamine, 2-ethylphenethylamine, 2-n-propylphenethylamine, 2-i-propylphenethylamine, 2-n-butylphenethylamine, 2-sec-butylphenethylamine, 2-t-butylphenethylamine, 3-methylphenethylamine, 3-i-propylphenethylamine, 3-i-propyl-4-methylphenethylamine, 3-t-butylphenethylamine, 4-methylphenethylamine, 4-i-propylphenethylamine, 2,6-dimethylphenethylamine, 2,3-dimethylphenethylamine, 2,4-dimethylphenethylamine, 3,4-diethylphenethylamine, 2,5-dimethylphenethylamine, 3,4-dimethylphenethylamine, 3,5-dimethylphenethylamine, 2,6-diethylphenethylamine, 2,6-di-i-propylphenethylamine, 2-methoxyphenethylamine, 2-ethoxyphenethylamine, 2-i-propoxyphenethylamine, 3-methoxyphenethylamine, 3,5-dimethoxyphenethylamine, 3-n-butoxyphenethylamine, 4-n-butoxyphenethylamine, 4-ethoxyphenethylamine, 3,4-dimethoxyphenethylamine, 2-methylthiophenethylamine, 2-ethylthiophenethylamine, 2-i-propylthiophenethylamine, 2-N,N-dimethylaminophenethylamine, 2-phenylphenethylamine, 3-phenylphenethylamine, 4-phenoxyphenethylamine, 2-cyclohexylphenethylamine, 2-cyclopentylphenethylamine, 2-nitrophenethylamine, 2,4-dinitrophenethylamine, 2-fluorophenethylamine, 2-chlorophenethylamine, 4-chlorophenethylamine, 2,3-dichlorophenethylamine, 3,4-dichlorophenethylamine, 2-i-propyl-4-nitrophenethylamine, 2-i-propyl-6-nitrophenethylamine, 2-hydroxyphenethylamine, 2-N,N-dimethylaminocarbonylphenethylamine, 2-N-acetylphenethylamine, 2-(1-ethylpropyl)phenethylamine, 2-i-propyl4-methylphenethylamine, 2-i-propyl-4-hydroxyphenethylamine, 2-i-propyl-4-chlorophenethylamine, 2-i-propyl-4-aminophenethylamine, 2-i-propyl-5-methylphenethylamine, 2-i-propyl-5-hydroxyphenethylamine, 2-i-propyl-5-chlorophenethylamine, 4-chloro-3-methylphenethylamine, 3,4-methylenedioxyphenethylamine or the like.

Process 2

[0061] This is a process for producing a compound of the formula (V) which comprises reacting an isothiocyanate of the compound of the formula (IV) with NH_2-R^1-OH.

[0062] This process can be carried out in an aprotic solvent (e.g., diethylether, tetrahydrofuran, dimethylformamide, benzene, toluene, dichloromethane, chloroform or the like).

[0063] The reaction temperature is preferably 0 to 100 °C, especially 0 °C to room temperature. The reaction time is 0.5 to 10 hours.

[0064] The amount of NH_2-R^1-OH wherein R^1 is optionally substituted alkylene is 1.0 to 1.5 mole equivalent to that of the compound of the formula (IV).

[0065] Examples of NH_2-R^1-OH include 2-aminoethanol, 2-amino-2-methylethanol, 2-amino-1-methylethanol, 2-amino-1,1-dimethylethanol, 3-aminopropanol, 3-amino-2,2-dimethylpropanol, 3-amino-1-methylpropanol, 3-amino-2-methylpropanol, 3-amino-3-methylpropanol, 3-amino-2,2-diethylpropanol, 1-aminomethyl-1-hydroxymethylcyclopropane, 1-aminomethyl- 1-(hydroxymethyl)cyclobutane, 2-(aminomethyl)cyclopentanol or the like.

Process 3

[0066] This is a process for producing a compound of the formula (VI) which comprises the cyclization of the compound of the formula (V).

[0067] A method of the cyclization includes 1) a method which comprises reacting with diethylazodicarboxylate (DEAD) and triphenylphosphine (Ph_3P), 2) a method which comprises reacting with hydrochloric acid or the like.

[0068] In the above 1), the reaction can be carried out in an aprotic solvent (e.g., diethylether, tetrahydrofuran, dimethylformamide, benzene, toluene, dichloromethane, chloroform or the like) with stirring for 0.5 to 5 hours at 0 °C to room temperature. The amount of diethylazodicarboxylate (DEAD) and triphenylphosphine (Ph_3P) are 1.0 to 1.5 mole equivalent to that of the compound (V).

[0069] In the above 2), the reaction can be carried out in concentrated hydrochloric acid with refluxing for 0.5 to 10 hours.

Process 4

[0070] This is a process for producing a compound of the formula (II) which comprises introducing R^2 (a group of the formula: -C(=R^5)-R^6 or a group of the formula: -SO_2R^7 wherein R^5 is O or S, R^6 is alkyl, alkoxy, alkylthio, optionally

substituted amino, optionally substituted aralkyloxy, optionally substituted aralkylthio, optionally substituted aralkylamino, alkoxyalkyl, alkylthioalkyl or optionally substituted aminoalkyl, R^7 is alkyl, optionally substituted amino, optionally substituted aryl or optionally substituted heteroaryl, to the compound of the formula (VI).

[0071] This process can be carried out by reacting with a compound of the formula: $X\text{-}C(=R^5)\text{-}R^6$ wherein R^5 and R^6 are as defined above and X is halogen in the presence of a base (e.g., triethylamine, pyridine, N,N-dimethylaminopyridine or the like). This process can be carried out under generally known conditions of N-acylation. For example, the reaction can be carried out in an aprotic solvent (e.g., diethylether, tetrahydrofuran, dimethylformamide, benzene, toluene, dichloromethane, chloroform or the like) with stirring at 0 to 100 °C for 0.5 to 10 hours.

[0072] A thioic acid ester, a compound wherein R^5 is S, R^6 is alkylthio or optionally substituted aralkylthio can be prepared by reacting with carbon dioxide (CS_2) in the presence of a base (e.g., sodium hydride or the like), and reacting with halogenated alkyl (e.g., methyl iodide, ethyl iodide or the like) or halogenated aralkyl (e.g., benzylbromide or the like). The reaction can be carried out in an aprotic solvent (e.g., diethylether, tetrahydrofuran, dimethylformamide, benzene, toluene, dichloromethane, chloroform or the like) with stirring at 0 °C to room temperature.

[0073] When R^2 to be introduced is a group of the formula: $-SO_2R^7$ wherein R^7 is alkyl, optionally substituted amino, optionally substituted aryl or optionally substituted heteroaryl, the compound of the formula (VI) can be reacted with a compound of the formula: R^7SO_2X wherein X is halogen or the like in the presence of a base.

[0074] A prodrug is a derivative which is converted to a pharmaceutically active compound of the present invention under a physiological condition. Method for the selection and process of an appropriate prodrug derivative are described in the literature such as Design of Prodrugs, Elsevier, Amsterdam 1985.

[0075] A prodrug of the present invention can he prepared by introducing a leaving group to substituents on ring A which are substitutable (e.g., amino, hydroxy or the like). Examples of a prodrug derived form a compound having an amino group includes carbamate derivatives (e.g., methylcarbamate, cyclopropylmethylcarbamate, t-butylcarbamate, benzylcarbamate or the like), amide derivatives (e.g., formamide, acetamide or the like), N-alkyl derivative (e.g., N-allylamine, N-methoxymethylamine or the like) or the like. Examples of a prodrug derived form a compound having hydroxy group include ether derivatives (methoxymethylether, methoxyethoxymethylether or the like), ester derivatives (e.g., acetate, pivaloate, benzoate or the like) or the like.

[0076] Examples of a pharmaceutically acceptable salt include basic salts (e.g., alkali metal salts such as sodium or potassium salts; alkaline-earth metal salts such as calcium or magnesium salts; ammonium salts; aliphatic amine salts such as trimethylamine, triethylamine, dicyclohexylamine, ethanolamine, diethanolamine, triethanolamine or procaine salts; aralkyl amine salts such as N,N-dibenzylethylenediamine salts; heterocyclic aromatic amine salts such as pyridine salts, picoline salts, quinoline salts or isoquinoline salts; quaternary ammonium salts such as tetramethylammonium salts, tetraethylammonium salts, benzyltrimethylammonium salts, benzyltriethylammonium salts, benzyltributylammonium salts, methyltrioctylammonium salts or tetrabutylammonium salts; and basic amino acid salts such as arginine salts or lysine salts). Acid addition salts include, for example, mineral acid salts such as hydrochlorides salts, sulfates salts, nitrate salts, phosphates salts, carbonates salts, hydrogen carbonates salts or perchlorates salts; organic acid salts such as acetates, propionates, lactates, maleates, fumarates, tartrates, malates, succinates, or ascorbates; sulfonates such as methanesulfonates, isethionates, benzenesulfonates, or p-toluenesulfonates; and acidic amino acid salts such as aspartates or glutamates.

[0077] A solvate includes a solvate of the compound of the formula (I) or (II), a prodrug of itself or a pharmaceutically acceptable salt thereof, for example, monosolvate, disolvate, monohydrate, dihydrate or the like.

[0078] The compound of the present invention has a binding activity to the cannabinoid type 2 receptor (CB2R), and selectively binds to the cannabinoid type 2 receptor (CB2R) to exhibit an antagonistic activity or agonistic activity to CB2R, especially an agonistic activity to CB2R.

[0079] Since the compound of the present invention does not have a binding activity to the cannabinoid type 1 receptor (CB1R), the present compound neither causes side effects on the central nervous system such as illusion or the drug dependence associated with the cannabinoid type 1 receptor.

[0080] Therefore, the compound of the present invention can be used for treating or preventing diseases associated with the cannabinoid type 2 receptor (CB2R). For example, Proc. Natl. Acad. Sci. USA 96, 14228-14233. discloses that CB2R agonists have an anti-inflammatory activity and analgesic activity. Nature, 1998, 349, 277-281 discloses that CB2R agonists have an analgesic activity. European Journal of Pharmacology 396 (2000) 85-92 discloses that CB2R antagonists have an analgesic activity.

[0081] The compound of the present invention suppresses an activation of cells in immunocyte or phlogocyte to exhibit an activity to the peripheral cell system (e.g., an immunosuppressive activity, an anti-inflammatory activity and an analgesic activity). Thus, the present compounds can be used as anti-inflammatory agents, antiallergenic agents, analgesic agents, immune deficiency treating agents, immunosuppressive agents, immunomodulating agents, autoimmune disease treating agents, chronic rheumatoid arthritis treating agents, multiple sclerosis treating agents or the like.

[0082] Agonists to the cannabinoid type 2 receptor are known to suppress nephritis caused by rat Thy-1 antibody in WO97/29079. Therefore, the present compounds are useful as nephritis treating agents.

[0083] When using a compound of the present invention in treatment, it can be formulated into ordinary formulations for oral and parenteral administration. A pharmaceutical composition containing a compound of the present invention can be in the form for oral and parenteral administration. Specifically, it can be formulated into formulations for oral administration such as tablets, capsules, granules, powders, syrup, and the like; those for parenteral administration such as injectable solution or suspension for intravenous, intramuscular or subcutaneous injection, inhalant, eye drops, nasal drops, suppositories, or percutaneous formulations such as ointment.

[0084] In preparing the formulations, carriers, excipients, solvents and bases known to one ordinary skilled in the art may be used. Tablets are prepared by compressing or formulating an active ingredient together with auxiliary components. Examples of usable auxiliary components include pharmaceutically acceptable excipients such as binders (e. g., cornstarch), fillers (e.g., lactose, microcrystalline cellulose), disintegrates (e.g., starch sodium glycolate) or lubricants (e.g., magnesium stearate). Tablets may be coated appropriately. In the case of liquid formulations such as syrups, solutions or suspensions, they may contain suspending agents (e.g., methyl cellulose), emulsifiers (e.g., lecithin), preservatives and the like. In the case of injectable formulations, it may be in the form of solution or suspension, or oily or aqueous emulsion, which may contain suspension-stabilizing agent or dispensing agent, and the like. In the case of an inhalant, it is formulated into a liquid formulation applicable to an inhaler. In the case of eye drops, it is formulated into a solution or a suspension.

[0085] Although an appropriate dosage of the present compound varies depending on the administration route, age, body weight, sex, or conditions of the patient, and the kind of drug(s) used together, if any, and should be determined by the physician in the end, in the case of oral administration, the daily dosage can generally be between about 0.01 - 100 mg, preferably about 0.01 - 10 mg, more preferably about 0.01 - 1 mg, per kg body weight. In the case of parenteral administration, the daily dosage can generally be between about 0.001 - 100 mg, preferably about 0.001 - 1 mg, more preferably about 0.001 - 0. 1 mg, per kg body weight. The daily dosage can be administered in 1 - 4 divisions.

Example

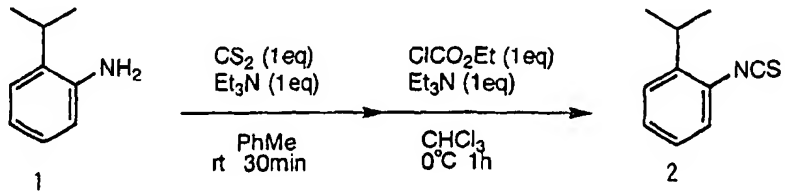
[0086] The following Examples are provided to further illustrate the present invention and are not to be construed as limiting the scope.

[0087] The meaning of each abbreviation are shown as follows.

Me: methyl, Et: ethyl, Pr: propyl, Pr^i: i-propyl,
Bu: butyl, Bu^i: i-butyl, Bu^s: sec-butyl,
Bu^t: t-butyl
Ph: phenyl, Ac: acetyl, Bn: benzyl
DMF: N,N-dimethylformamide, THF: tetrahydrofuran,
DEAD: diethyl azodicarboxylate,

Reference Example 1-1 Preparation of (2-isopropylphenyl)isothiocyanate (Compound 2).

[0088]

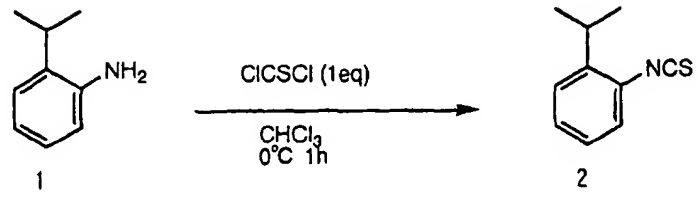


1 2

[0089] To a mixture of 2-isopropylaniline (5.00 g), triethylamine (3.74 g) and toluene (10 ml) was added dropwise for 10 minutes carbon dioxide (2.81 g). The mixture was stirred at room temperature for 1 hour and kept stationary for 12 hours. The reaction mixture was concentrated under reduced pressure. Dichloromethane (20 ml) and triethylamine (3.74 g) were added thereto. To the solution was added under ice-cooling for 10 minutes ethyl chlorocarbonate (4.01 g). The mixture was stirred at room temperature for 1 hour. To the reaction mixture was added 10% hydrochloric acid (20 ml). The mixture was extracted with dichloromethane (60 ml), dried over anhydrous magnesium sulfate and concentrated under reduced pressure to give (2-isopropylphenyl)isothiocyanate (6.55 g, yield: 99 %) as yellow oil.
^{1}H-NMR (δ ppm TMS / $CDCl_3$) 1.25(6H, d, J=6.7), 3.25(1H, q, J=6.7), 7.14-7.30(4H, m).

Reference Example 1-2 Preparation of (2-isopropylphenyl)isothiocyanate (Compound 2).

[0090]



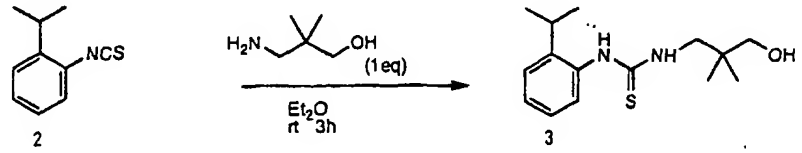
1 2

[0091] To a solution of 2-isopropylaniline (1.81 g) in diethylether (20 ml) was added dropwise under ice-cooling for 10 minutes thiophosgene (1.54 g). The mixture was stirred at room temperature for 1 hour.

[0092] To the reaction solution was added water (30 ml). The mixture was extracted with diethylether (60 ml), dried over anhydrous magnesium sulfate and concentrated under reduced pressure to give (2-isopropylphenyl)isothiocyanate (2.35 g, yield: 99 %) as brown oil.

Reference Example 2 Preparation of N-(2-isopropylphenyl)-N'-(1-hydroxy-2,2-dimethyl)propylthiourea (Compound 3).

[0093]



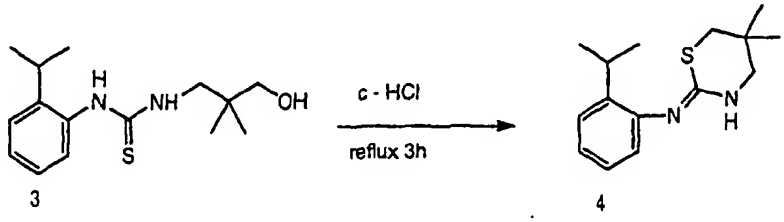
2 3

[0094] To a solution of (2-isopropylphenyl)isothiocyanate (3.30 g) in diethylether (20 ml) was added 3-amino-2,2-dimethylpropanol (1.92 g). The mixture was stirred at room temperature for 1 hour and concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (n-hexane/ethyl acetate) to give N-(2-isopropylphenyl)-N'-(1-hydroxy-2,2-dimethyl)propylthiourea (4.60 g, yield: 88 %) as yellow oil.

^{1}H-NMR (δ ppm TMS / $CDCl_3$) 0.82(6H, s), 1.25(6H, d, J=6.7), 3.11(1H, q, J=6.7), 3.25(2H, s), 3.55(2H, d, J=6.3), 6.05(1H, m), 7.17-7.40(4H, m).

Reference Example 3 Preparation of 2-(2-isopropylphenyl)imino-5,5-dimethyl-1,3-thiazine (Compound 4).

[0095]



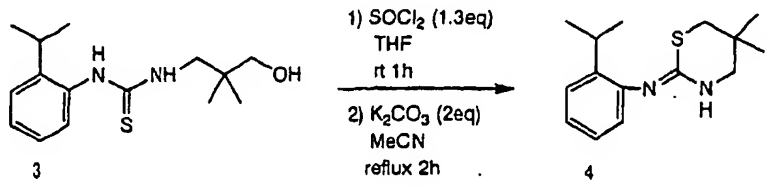
3 4

[0096] To N-(2-isopropylphenyl)-N'-(1-hydroxy-2,2-dimethyl)propylthiourea (10.37 g) was added concentrated hydrochloric acid (5 ml). The mixture was refluxed for 3 hours. The reaction solution was cooled to room temperature and poured into an aqueous solution of 20 % sodium hydroxide (25 ml). The precipitated crystal was filtered and

recrystallized with ethyl acetate to give 2-(2-isopropylphenyl)imino-5,5-dimethyl-1,3-thiazine (4.80 g, yield: 50 %) as a white crystal.
M.p. 155-157 °C
^{1}H-NMR (δ ppm TMS / $CDCl_3$) 1.15(6H, s), 1.20(6H, d, J=6.7), 2.67(2H, s), 3.09(2H, s), 3.15.(1H, q, J=6.7), 6.88(1H, m), 7.05-7.11(2H, m), 7.20(1H, m).

Reference Example 4 Preparation of 2-(2-isopropylphenyl)imino-5,5-dimethyl-1,3-thiazine (Compound 4).

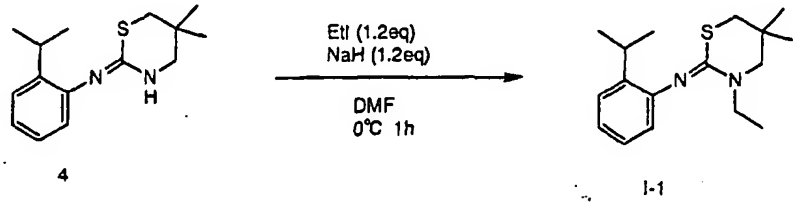
[0097]



[0098] To a solution of N-(2-isopropylphenyl)-N'-(1-hydroxy-2,2-dimethyl)propylthiourea (1.00 g) in tetrahydrofuran (6 ml) was added dropwise thionylchloride (0.60 g). The mixture was stirred at room temperature for 1 hour and concentrated under reduced pressure. To the solution were added acetonitrile (20 ml) and potasium carbonate (0.93 g). The mixture was refluxed for 2 hours. To the solution was added water (40 ml). The mixture was extracted with dichloromethane (60 ml), dried over anhydrous magnesuim sulfate and concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (n-hexane/ethyl acetate) to give 2-(2-isopropylphenyl)imino-5,5-dimethyl-1,3-thiazine (0.45g, yield: 48 %) as a white crystal.
[0099] The following Examples 1 to 5 were carried out by using 2-(2-isopropylphenyl)imino-5,5-dimethyl-1,3-thiazine prepared in Reference Example 3 and 4.

Example 1 Preparation of 3-ethyl-2-(2-isopropylphenyl)imino-5,5-dimethyl-1,3-thiazine (Compound I-1).

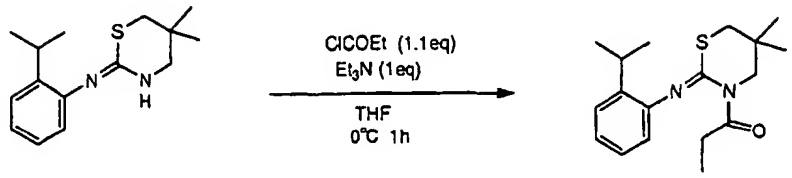
[0100]



[0101] To a solution of 2-(2-isopropylphenyl)imino-5,5-dimethyl-1,3-thiazine (0.26 g) in N,N-dimethylformamide (2 ml) was added under ice-cooling 60 % sodium hydride (0.05 g). The mixture was stirred for 30 minutes. Ethyliodide (0.17 g) was added thereto. The mixture was stirred at room temperature for 2 hours. To a reaction mixture was added water (30 ml), extracted with diethylether (60 ml), dried over anhydrous magnesium sulfate and concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (n-hexane/ethyl acetate) to give 3-ethyl-2-(2-isopropylphenyl)imino-5,5-dimethyl-1,3-thiazine (0.21g, yield: 71%) as colorless oil.
^{1}H-NMR (δ ppm TMS / $CDCl_3$) 1.13 (6H, s), 1.20 (6H, d, J = 6.9), 1.25 (3H, t, J = 7.4), 2.61 (2H, s),3.05 (2H,s), 3.17 (1H, m), 3.64 (2H, q, J = 6.9), 6.72-6.80 (1H, m), 6.98-7.07 (2H, m), 7.20-7.32 (1H, m).

Example 2 Preparation of 2-(2-isopropylphenyl)imino-3-propionyl-5,5-dimethyl-1,3-thiazine (Compound I-2).

[0102]

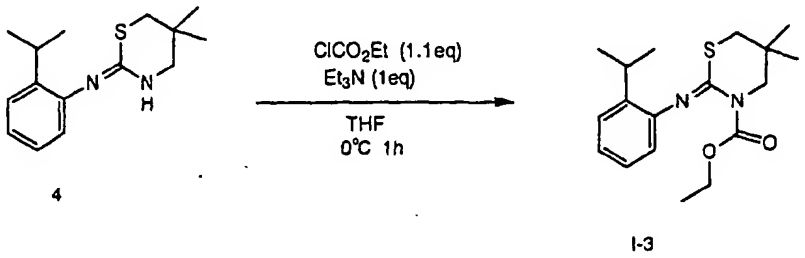


4 I-2

[0103] To a mixture of 2-(2-isopropylphenyl)imino-5,5-dimethyl-1,3-thiazine (0.26 g), triethylamine (0.15 g) and dichloromethane (5 ml) was added dropwise for 5 minutes propionylchloride (0.13 g). The mixture was stirred at room temperature for 2 hours. To the solution was added water (30 ml). The mixture was extracted with diethylether (60 ml), dried over anhydrous magnesium sulfate and concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (n-hexane/ethyl acetate) to give 2-(2-isopropylphenyl)imino-3-propionyl-5,5-dimethyl-1,3-thiazine (0.18g, yield: 56 %) as colorless oil.
^{1}H-NMR (δ ppm TMS / $CDCl_3$)1.14 (6H, s), 1.20 (6H, d, J = 6.9), 1.22 (3H, t, J = 7.4), 2.60 (2H, s), 2.95 (2H, q, J = 7.4), 2.96 (1H, q, J = 6.9), 3.73 (2H, s), 6.73-6.78 (1H, m), 7.10-7.17 (2H, m), 7.25-7.32 (1H, m).

Example 3 Preparation of 3-(ethoxycarbonyl)-2-(2-isopropylphenyl)imino-5,5-dimethyl-1,3-thiazine (Compound I-3).

[0104]

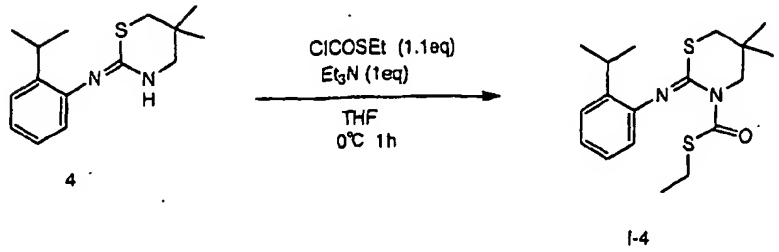


4 I-3

[0105] To a mixture of 2-(2-isopropylphenyl)imino-5,5-dimethyl-1,3-thiazine (0.26 g), triethylamine (0.15 g) and dichloromethane (5 ml) was added dropwise for 5 minutes ethyl chlorocarbonate (0.13 g). The mixture was stirred at room temperature for 2 hours. To the solution was added water (30 ml). The mixture was extracted with diethylether (60 ml), dried over anhydrous magnesium sulfate and concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (n-hexane/ethyl acetate) to give 3-(ethoxycarbonyl)-2-(2-isopropylphenyl)imino-5,5-dimethyl-1,3-thiazine (0.23 g, yield: 68 %) as a white crystal. M.p. 84-86 °C.
^{1}H-NMR (δ ppm TMS / $CDCl_3$) 1.16 (6H, s), 1.21 (6H, d, J = 6.9), 1.36 (3H, t, J = 7.1), 2.59 (2H, s), 3.17 (1H, q, J = 6.9), 3.65 (2H, s), 4.32 (2H, q, J = 7.1), 6.74-6.78 (1H,m), 7.12-7.16 (2H, m), 7.30-7.36 (1H, m).

Example 4 Preparation of 3-(ethylthiocarbonyl)-2-(2-isopropylphenyl)imino-5,5-dimethyl-1,3-thiazine (Compound I-4).

[0106]

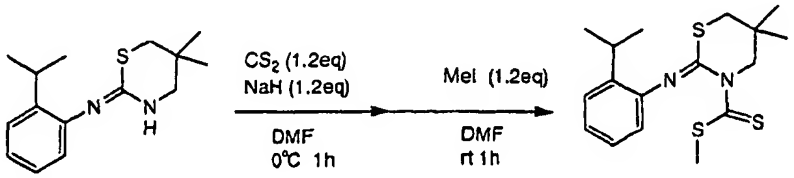


4 I-4

[0107] To a mixture of 2-(2-isopropylphenyl)imino-5,5-dimethyl-1,3-thiazine (1.00 g), triethylamine (0.58 g) and dichloromethane (5 ml) was added dropwise for 5 minutes ethyl chlorothiocarbonate (0.56 g). The mixture was stirred at room temperature for 1 hour. To the solution was added water (30 ml). The mixture was extracted with diethylether (60 ml), dried over anhydrous magnesium sulfate and concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (n-hexane/ethyl acetate) to give 3-(ethylthiocarbonyl)-2-(2-isopropylphenyl)imino-5,5-dimethyl-1,3-thiazine (0.74 g, yield: 56 %) as colorless oil.
^{1}H-NMR (δ ppm TMS / $CDCl_3$)1.16 (6H, s), 1.21 (6H, d, J = 6.9), 1.36 (3H, t, J = 7.1), 2.63 (2H, s), 2.89 (2H, q, J = 7.1), 3.15 (1H, q, J = 6.9), 3.77 (2H, s), 6.79-6.85 (1H,m),7.12-7.16 (2H, m), 7.30-7.36 (1H, m).

Example 5 Preparation of 2-(2-isopropylphenyl)imino-3-(methylthio)thiocarbonyl-5,5-dimethyl-1,3-thiazine (Compound I-5).

[0108]



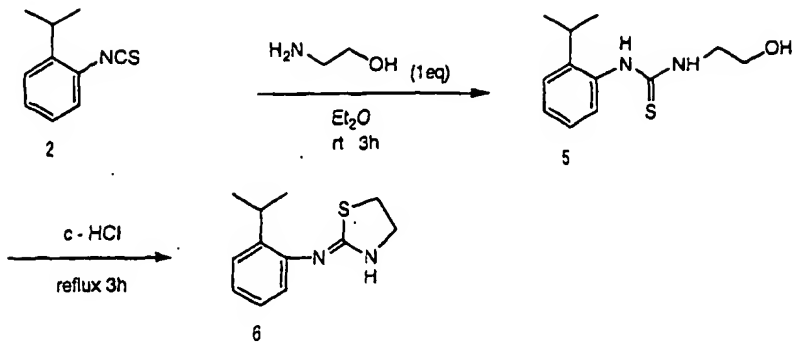
4 I-5

[0109] To a mixture of 2-(2-isopropylphenyl)imino-5,5-dimethyl-1,3-thiazine (0.26 g), carbon dioxide (0.09 g) and N, N-dimethylformamide (2 ml) was added under ice-cooling 60 % sodium hydride (0.05 g). The mixture was stirred for 30 minutes. Methyliodide (0.17 g) was added thereto. The mixture was stirred at room temperature for 2 hours. To the solution was added water (30 ml), extracted with diethylether (60 ml), dried over anhydrous magnesium sulfate and concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (n-hexane/ethyl acetate) to give 2-(2-isopropylphenyl)imino-3-(methylthio)thiocarbonyl-5,5-dimethyl-1,3-thiazine (0.14 g, yield: 40 %) as a yellow crystal. M.p. 77-79 °C.
^{1}H-NMR (δ ppm TMS / $CDCl_3$)1.20 (6H, d, J = 6.9), 1.23 (6H, s), 2.65 (3H, s), 2.68 (2H, s), 3.11 (1H, q, J = 6.9), 4.51 (2H, s), 6.83-6.90 (1H, m), 7.11-7.18 (2H, m), 7.28-7.35 (1H, m).

[0110] The following Reference Example 5 was carried out in accordance with Reference Example 2 and 3.

Reference Example 5 Preparation of 2-(2-isopropylphenyl)imino-1,3-thiazolidine (Compound 6).

[0111]

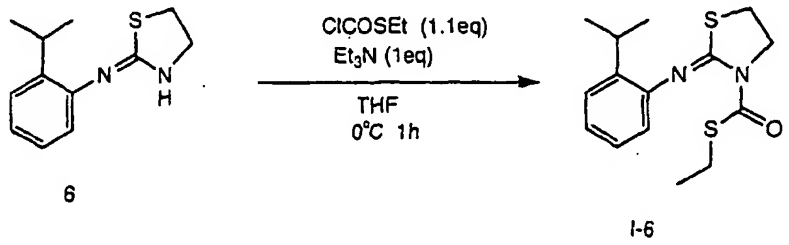


[0112] To a solution of (2-isopropylphenyl)isothiocyanate (2.00 g) in diethylether (20 ml) was added 2-aminoethanol (0.69 g). The mixture was stirred at room temperature for 1 hour and concentrated under reduced pressure. To the obtained oil was added concentrated hydrochloric acid (5 ml). The mixture was refluxed for 3 hours. The reaction mixture was cooled to room temperature and poured into an aqueous solution of 20 % sodium hydroxide (25 ml). The mixture was extracted with dichloromethane (60 ml), dried over anhydrous magnesium sulfate and concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (n-hexane/ethyl acetate) to give 2-(2-isopropylphenyl)imino-1,3-thiazolidine (1.80 g, yield: 73 %) as a white crystal. M.p. 76-77 °C.
^{1}H-NMR (δ ppm TMS / $CDCl_3$) 1.20(6H, d, J=6.7), 3.15(1H, q, J=6.7), 3.27(2H, t, J = 6,7), 3.67(2H, t, J = 6.7), 6.95-6.99 (1H, m), 7.05-7.19(2H, m), 7.22-7.26(1H, m).

[0113] The following Example 6 and 7 were carried out by using 2-(2-isopropylphenyl)imino-1,3-thiazolidine prepared in Reference Example 5.

Example 6 Preparation of 3-(ethylthiocarbonyl)-2-(2-isopropylphenyl)imino-1,3-thiazolidine (Compound I-6).

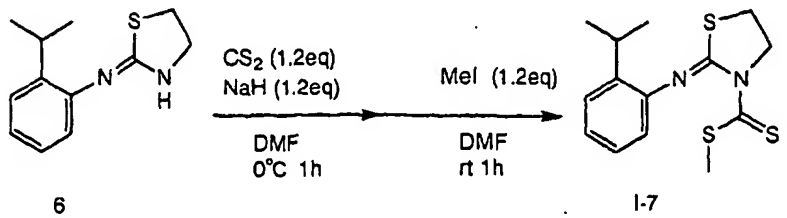
[0114]



[0115] To a mixture of 2-(2-isopropylphenyl)imino-1,3-thiazolidine (0. 25 g), triethylamine (0.15 g) and dichloromethane (5 ml) was added dropwise for 5 minutes ethyl chlorothiocarboxylate (0.15 g). The mixture was stirred for 2 hours. To the solution was added water (30 ml). The mixture was extracted with diethylether (60 ml), dried over anhydrous magnesium sulfate and concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (n-hexane/ethyl acetate) to give 3-(ethylthiocarbonyl)-2-(2-isopropylphenyl)imino-1,3-thiazolidine (0.27 g, yield: 77 %) as a white crystal. M.p. 79-81 °C.
^{1}H-NMR (δ ppm TMS / $CDCl_3$) 1.20 (6H, d, J = 6.9), 1.30 (3H, t, J = 7.4), 2.90 (2H, t, J = 7.4), 3.15 (2H, t, J = 7.4), 3.20 (1H, q, J = 6.9), 4.31 (2H, t, J = 7.4), 6.79-6.82 (1H, m), 7.07-7.16 (2H, m), 7.28-7.32 (1H, m).

Example 7 Preparation of 2-(2-isopropylphenyl)imino-3-(methylthio)thiocarbonyl-1,3-thiazolidine (Compound I-7).

[0116]

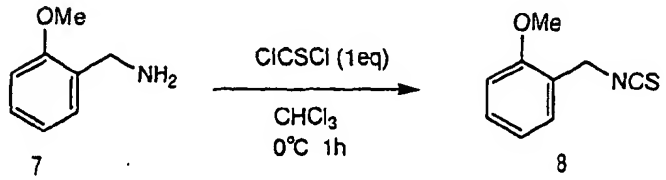


6 I-7

[0117] To a mixture of 2-(2-isopropylphenyl)imino-1,3-thiazolidine (0.22 g), carbon disulfide (0.09 g) and N,N-dimethylformamide (2 ml) was added under ice-cooling 60 % sodium hydride (0.05 g). The mixture was stirred for 30 minutes. Methyliodide (0.17 g) was added thereto. The mixture was stirred at room temperature for 2 hours. To the mixture was added water (30 ml). The mixture was extracted with diethylether (60 ml), dried over anhydrous magnesium sulfate and concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (n-hexane/ethyl acetate) to give 2-(2-isopropylphenyl)imino-3-(methylthio)thiocarbonyl-1,3-thiazolidine (0.14 g, yield: 45 %) as colorless oil. ^{1}H-NMR (δ ppm TMS / $CDCl_3$) 1.23 (6H, d, J = 6.9), 2.65 (3H, s), 2.90 (2H, t, J = 7.4), 3.20 (1H, q, J = 6.9), 4.45 (2H, t, J = 7.4), 6.79-6.82 (1H, m), 7.07-7.16 (2H, m), 7.28-7.32 (1H, m).

Reference Example 6 Preparation of (2-methoxybenzyl)isothiocyanate (Compound 8).

[0118]

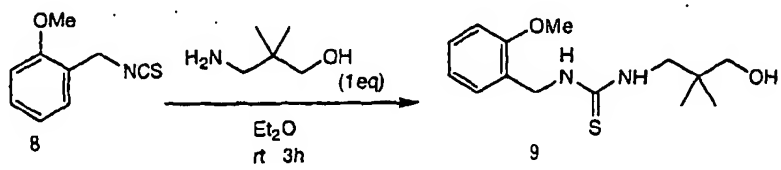


7 8

[0119] To a solution of 2-methoxybenzylamine (1.80 g) in diethylether (20 ml) was added dropwise under ice-cooling for 10 minutes thiophosgene (1.54 g). The mixture was stirred at room temperature for 1 hour. To the reaction solution was added water.(30 ml), extracted with diethylether (60 ml), dried over anhydrous magnesium sulfate and concentrated under reduced pressure to give (2-methoxybenzyl)isothiocyanate (2.35 g, yield: 99 %) as brown oil.
^{1}H-NMR (δ ppm TMS / $CDCl_3$) 3.86(3H, s), 4.70(2H, s), 6.88 (1H, d, J = 7.4), 6.98(1H, t, J = 7.4), 7.24-7.30(2H, m).

Reference Example 7 Preparation of N-(2-methoxybenzyl)-N'-(1-hydroxy-2,2-dimethyl)propylthiourea (Compound 9).

[0120]



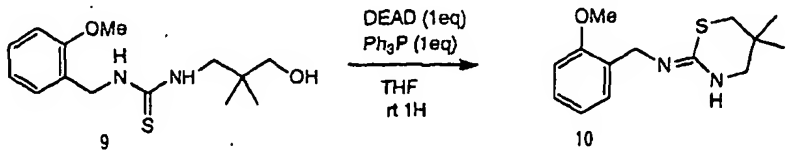
8 9

[0121] To a solution of (2-methoxybenzyl)isothiocyanate (2.35 g) in diethylether (20 ml) was added 3-amino-2,2-dimethylpropanol (1.34 g). The mixture was stirred at room temperature for 1 hour. The mixture was concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (n-hexane/ethyl ac-

etate) to give N-(2-methoxybenzyl)-N'-(1-hydroxy -2,2-dimethyl)propylthiourea (3.70 g, yield: 99 %) as colorless oil.
^{1}H-NMR (δ ppm TMS / $CDCl_3$) 0.82(6H, s), 3.25(2H, s), 3.55(2H, d, J=6.3), 3.86(3H, s), 4.70(2H, s), 6.50(1H, brs), 6.88(1H, d, J = 7.4), 6.95(1H, t, J = 7.4), 7.24-7.30(2H, m).

Reference Example 8 Preparation of 2-(2-methoxybenzyl)imino-5,5-dimethyl-1,3-thiazine (Compound 10).

[0122]



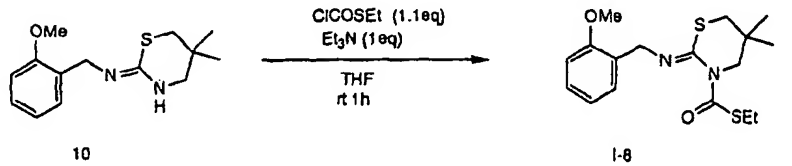
9 10

[0123] To a mixture of N-(2-methoxybenzyl)-N'-(1-hydroxy-2,2-dimethyl)propylthiourea (3.70 g), triphenylphosphine (3.44 g) and tetrahydrofuran (20 ml) was added dropwise for 10 minutes diethyl azodicarboxylate (2.28 g). The mixture was stirred at room temperature for 2 hours. To the solution was added water (40 ml). The mixture was extracted with dichloromethane (90 ml), dried over anhydrous magnesium sulfate and concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (n-hexane/ethyl acetate) to give 2-(2-methoxybenzyl)imino-5,5-dimethyl-1,3-thiazine (0.87 g, yield: 25 %) as colorless oil.
^{1}H-NMR (δ ppm TMS / $CDCl_3$) 1.05(6H, s,), 2.75(2H, s), 3.23(2H, s), 3.83(3H, s), 4.41(2H, s), 6.86-6.95(1H, m), 7.20-7.30(1H, m), 7.44-7.48 (2H, m).

[0124] The following Examples 8 and 9 were carried out by using 2-(2-methoxybenzyl)imino-5,5-dimethyl-1,3-thiazine prepared in Reference Example 8.

Example 8 Preparation of 3-(ethylthiocarbonyl)-2-(2-methoxybenzyl)imino-5,5-dimethyl-1,3-thiazine (Compound I-8).

[0125]

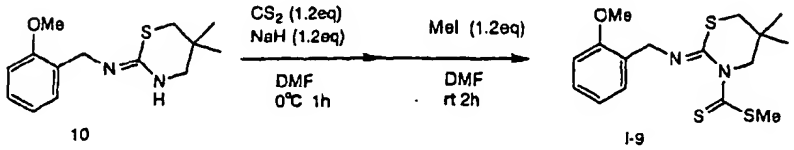


10 I-8

[0126] To a mixture of 2-(2-methoxybenzyl)imino-5,5-dimethyl-1,3-thiazine (0.28 g), triethylamine (0.15g) and dichloromethane (5 ml) was added dropwise for 5 minutes ethyl chlorothiocarboxylate (0.17 g). The mixture was stirred at room temperature for 1 hour. To the reaction solution was added water (30 ml), extracted with diethylether (60 ml), dried over anhydrous magnesium sulfate and concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (n-hexane/ethyl acetate) to give 3-(ethylthiocarbonyl)-2-(2-methoxybenzyl)imino-5,5-dimethyl-1,3-thiazine (0.20 g, yield: 57 %) as colorless oil.
^{1}H-NMR (δ ppm TMS / $CDCl_3$) 1.15 (6H, s), 1.25 (3H, t, J = 7.4), 2.69 (2H, s), 2.83 (2H, q, J = 7.4), 3.69 (2H, s), 3.84 (3H, s), 4.61 (2H, s), 6.86 (1H, d, J = 8.2), 6.96 (1H, t, J = 8.2), 7.26 (1H, t, J = 8.2), 7.55 (1H, t, J = 8.2).

Example 9 Preparation of 2-(2-methoxybenzyl)imino-3-(methylthio)thiocarbonyl-5,5-dimethyl-1,3-thiazine (Compound I-9).

[0127]

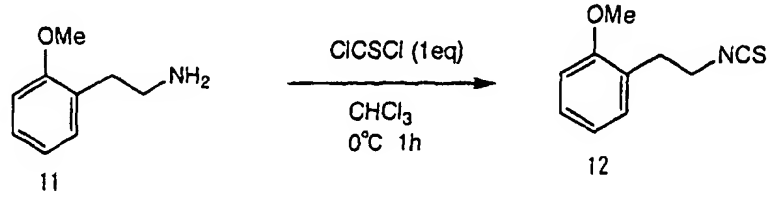


10 I-9

[0128] To a mixture of 2-(2-methoxybenzyl)imino-5,5-dimethyl-1,3-thiazine(0.27g), carbon disulfide (0.09 g) and N, N-dimethylformamide (2 ml) was added under ice-cooling 60 % sodium hydride (0.05 g). The mixture was stirred for 30 minutes. Methyl iodide (0.17 g) was added thereto. The mixture was stirred at room temperature for 2 hours. To the solution was added water (30 ml). The mixture was extracted with diethylether (60 ml), dried over anhydrous magnesium sulfate and concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (n-hexane/ethyl acetate) to give 2-(2-methoxybenzyl)imino-3-(methylthio)thiocarbonyl-5,5-dimethyl-1,3-thiazine (0.20 g, yield: 57 %) as colorless oil.
^{1}H-NMR (δ ppm TMS / $CDCl_3$) 1.25 (6H, s), 2.56 (3H, s), 2.72 (2H, s), 3.85 (3H, s), 4.43 (2H, s), 4.63 (2H, s), 6.86-6.88 (2H, m), 7.20-7.30 (1H, m), 7.44-7.48 (1H, m).

Reference Example 9 Preparation of (2-methoxyphenethyl)isothiocyanate (Compound 12).

[0129]

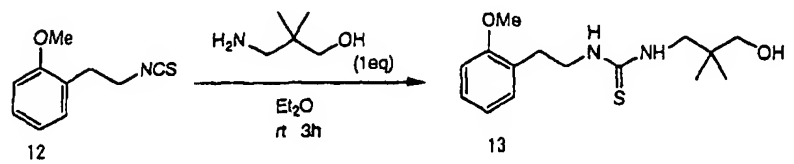


11 12

[0130] To a solution of 2-methoxyphenethylamine (1.98 g) in diethylether (20 ml) was added dropwise under ice-cooling thiophosgene (1.54 g). The mixture was stirred at room temperature for 1 hour. To the solution was added water (30 ml). The mixture was extracted with diethylether (60 ml), dried over anhydrous magnesium sulfate and concentrated under reduced pressure to give (2-methoxyphenethyl)isothiocyanate (1.80g, yield: 71 %) as brown oil.
^{1}H-NMR (δ ppm TMS / $CDCl_3$) 3.00(2H, t, J = 7.4), 3.70(2H, t, J = 7.4), 3.86(3H, s), 6.88-6.95(2H, m), 7.15(1H, d, J = 7.4), 7.24(1H, t, J = 7.4).

Reference Example 10 Preparation of N-(2-methoxyphenethyl)-N'-(1-hydroxy -2,2-dimethyl)propylthiourea (Compound 13).

[0131]



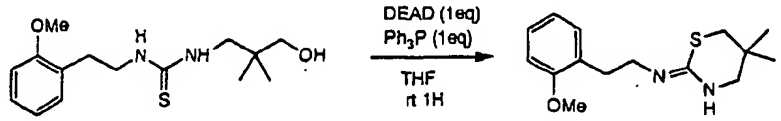
12 13

[0132] To a solution of (2-methoxyphenethyl)isothiocyanate (2.35 g) in diethylether (20 ml) was added 3-amino-2,2-dimethylpropanol (1.34 g). The mixture was stirred at room temperature for 1 hour. The mixture was concentrated

under reduced pressure. The obtained residue was purified by silica gel column chromatography (n-hexane/ethyl acetate) to give N-(2-methoxyphenethyl)-N'-(1-hydroxy -2,2-dimethyl)propylthiourea (2.45 g, yield 89 %) as colorless oil.
^{1}H-NMR (δ ppm TMS / $CDCl_3$) 0.82(6H, s), 2.90(2H, t, J = 7.4), 3.25(2H, s), 3.55(2H, d, J=6.3), 3.70(2H, t, J = 7.4), 3.86(3H, s), 6.50(1H, brs), 6.88-6.95(2H, m), 7.15(1H, m), 7.24(1H, m).

Reference Example 11 Preparation of 2-(2-methoxyphenethyl)imino-5,5-dimethyl-1,3-thiazine (Compound 14).

[0133]



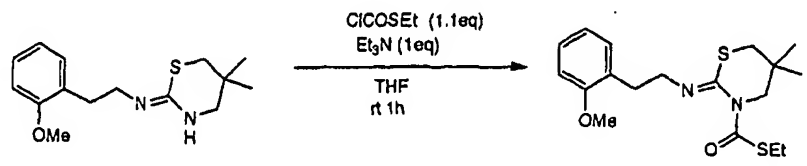
13 14

[0134] To a mixture of N-(2-methoxyphenethyl)-N'-(1-hydroxy-2,2-dimethyl)propylthiourea (2.40 g), triphenylphosphine (2.12 g) and tetrahydrofuran (20 ml) was added dropwise for 10 minutes diethyl azodicarboxylate (2.28 g). The mixture was stirred at room temperature for 2 hours. To the solution was added water (40 ml). The mixture was extracted with dichloromethane (90 ml), dried over magnesium sulfate and concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (n-hexane/ethyl acetate) to give 2-(2-methoxyphenethyl) imino-5,5-dimethyl-1,3-thiazine (0.70 g, yield: 31 %) as colorless oil.
^{1}H-NMR (δ ppm TMS / $CDCl_3$) 1.05(6H, s,), 2.72(2H, s), 2.80(2H, t, J = 7.4), 3.25(2H, s), 3.55(2H, d, J=6.3), 3.83(3H, s), 6.83-6.95(2H, m), 7.15(1H, m), 7.24(1H, m).

[0135] The following Examples 10 and 11 were carried out by using 2-(2-methoxyphenethyl)imino-5,5-dimethyl-1,3-thiazine prepared in Example 11.

Example 10 Preparation of 3-(ethylthiocarbonyl)-2-(2-methoxyphenethyl)imino-5,5-dimethyl-1,3-thiazine (Compound I-10).

[0136]

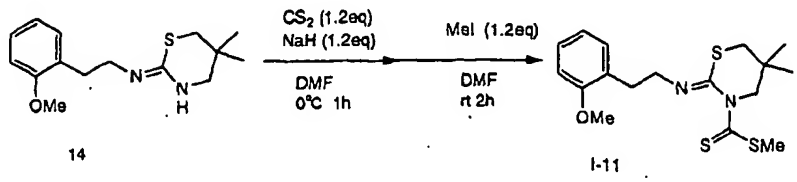


14 I-10

[0137] To a mixture of 2-(2-methoxyphenethyl)imino-5,5-dimethyl-1,3-thiazine (0.28g), triethylamine (0.15g) and dichloromethane (5 ml) was added dropwise for 3 minutes ethyl chlorothiocarbonate (0.15 g). The mixture was stirred at room temperature for 2 hours. To the solution was added water (30 ml). The mixture was extracted with diethylether (60 ml), dried over anhydrous magnesium sulfate and concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (n-hexane/ethyl acetate) to give 2-(2-methoxyphenethyl)imino-N-(ethylthiocarbamoyl)-5,5-dimethyl-1,3-thiazine (0.21 g, yield :60 %) as colorless oil.
^{1}H-NMR (δ ppm TMS / $CDCl_3$) 1.11 (6H, s), 1.26 (3H, t, J = 7.4), 2.61 (2H, s), 2.83 (2H, q, J = 7.4), 2.99-3.05 (2H, m), 3.61-3.66 (2H, m), 3.62 (2H, s), 3.82 (3H, s), 6.86-6.91 2H, m), 7.17-7.26 (2H, m).

Example 11 Preparation of 2-(2-methoxyphenethyl)imino-3-(methylthio)thiocarbonyl-5,5-dimethyl-1,3-thiazine (Compound I-11).

[0138]



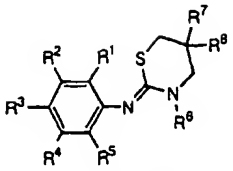
14 I-11

[0139] To a mixture of 1-(1-methoxyphenethyl)imino-5,5-dimethyl-1,3-thiazine (0.28 g), carbondisulfide (0.09 g) and N,N-dimethylformamide (2 ml) was added under ice-cooling 60 % sodium hydride (0.05 g). The mixture was stirred for 30 minutes. Methyliodide (0.17 g) was added thereto. The mixture was stirred at room temperature for 2 hours. To the solution was added water (30 ml). The mixture was extracted with diethylether (60 ml), dried over anhydrous magnesium sulfate and concentrated under reduced pressure. The obtained residue was chromatographed (n-hexane/ethyl acetate) to give 2-(2-methoxyphenethyl)imino-3-(methylthio)thiocarbonyl-5,5-dimethyl-1,3-thiazine (0.18 g, yield :50 %) as colorless oil.

^{1}H-NMR (δ ppm TMS / $CDCl_3$) 1.19 (6H, s), 2.55 (3H,s), 2.64 (2H, s), 3.05 (2H, t, J = 7.5), 3.66 (2H, t, J = 7.5), 3.84 (3H, s), 4.35 (2H, s), 6.84- 6.91 (2H, m), 7.17-7.30 (2H, m).

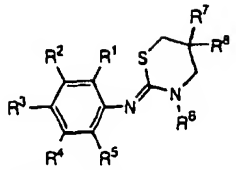
[0140] The compounds shown in the following tables were prepared in accordance with the above Example. The numbers of left column in Tables represent Compound No.

(Table 1)



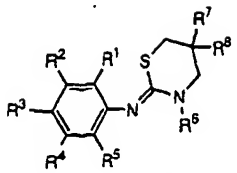
	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
I-16	H	H	H	H	H	COSEt	Me	Me
I-17	F	H	H	H	H	COSEt	Me	Me
I-18	Cl	H	H	H	H	COSEt	Me	Me
I-19	Me	H	H	H	H	COSEt	Me	Me
I-20	Et	H	H	H	H	COSEt	Me	Me
I-21	Pr	H	H	H	H	COSEt	Me	Me
I-22	Bu	H	H	H	H	COSEt	Me	Me
I-23	Bu^s	H	H	H	H	COSEt	Me	Me
I-24	Bu^t	H	H	H	H	COSEt	Me	Me
I-25	Ph	H	H	H	H	COSEt	Me	Me
I-26	CF_3	H	H	H	H	COSEt	Me	Me
I-27	OMe	H	H	H	H	COSEt	Me	Me
I-28	OEt	H	H	H	H	COSEt	Me	Me
I-29	OPr^i	H	H	H	H	COSEt	Me	Me
I-30	SMe	H	H	H	H	COSEt	Me	Me
I-31	SEt	H	H	H	H	COSEt	Me	Me
I-32	SPr^i	H	H	H	H	COSEt	Me	Me
I-33	NMe_2	H	H	H	H	COSEt	Me	Me
I-34	H	Pr^i	H	H	H	COSEt	Me	Me
I-35	H	H	Cl	H	H	COSEt	Me	Me
I-36	H	H	Pr^i	H	H	COSEt	Me	Me
I-37	H	H	NO_2	H	H	COSEt	Me	Me
I-38	Me	Me	H	H	H	COSEt	Me	Me
I-39	Me	H	Me	H	H	COSEt	Me	Me
I-40	Me	H	H	Me	H	COSEt	Me	Me
I-41	Me	H	H	H	Me	COSEt	Me	Me
I-42	H	Me	Me	H	H	COSEt	Me	Me
I-43	H	Me	H	Me	H	COSEt	Me	Me
I-44	Me	H	Cl	H	H	COSEt	Me	Me

(Table 2)



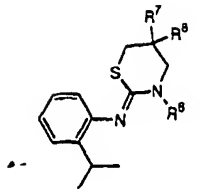
	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
I-45	Cl	H	Me	H	H	COSEt	Me	Me
I-46	Pr^i	H	NO_2	H	H	COSEt	Me	Me
I-47	Pr^i	H	H	H	NO_2	COSEt	Me	Me
I-48	NO_2	H	NO_2	H	H	COSEt	Me	Me
I-49	Pr	H	H	H	H	COSMe	Me	Me
I-50	Pr^i	H	H	H	H	COSMe	Me	Me
I-51	Bu^s	H	H	H	H	COSMe	Me	Me
I-52	H	Pr^i	H	H	H	COSMe	Me	Me
I-53	H	OMe	OMe	H	H	COSMe	Me	Me
I-54	H	$-OCH_2O-$		H	H	COSMe	Me	Me
I-55	H	OMe	OMe	OMe	H	COSMe	Me	Me
I-56	Et	H	H	H	H	CSSMe	Me	Me
I-57	Bu^s	H	H	H	H	CSSMe	Me	Me
I-58	CH_2OMe	H	H	H	H	CSSMe	Me	Me
I-59	CH(Me)OMe	H	H	H	H	CSSMe	Me	Me
I-60	OMe	H	H	H	H	CSSMe	Me	Me
I-61	OEt	H	H	H	H	CSSMe	Me	Me
I-62	SMe	H	H	H	H	CSSMe	Me	Me
I-63	SEt	H	H	H	H	CSSMe	Me	Me
I-64	SPr^i	H	H	H	H	CSSMe	Me	Me
I-65	SOMe	H	H	H	H	CSSMe	Me	Me
I-66	SO_2Me	H	H	H	H	CSSMe	Me	Me
I-67	SOEt	H	H	H	H	CSSMe	Me	Me
I-68	NMe_2	H	H	H	H	CSSMe	Me	Me
I-69	H	Pr^i	H	H	H	CSSMe	Me	Me
I-70	H	H	Cl	H	H	CSSMe	Me	Me

(Table 3)



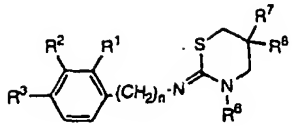
	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
I-71	Me	H	Me	H	H	CSSMe	Me	Me
I-72	Me	H	H	Me	H	CSSMe	Me	Me
I-73	Me	H	H	H	Me	CSSMe	Me	Me
I-74	H	Me	Me	H	H	CSSMe	Me	Me
I-75	H	Me	H	Me	H	CSSMe	Me	Me
I-76	OMe	OMe	H	H	H	CSSMe	Me	Me
I-77	H	OMe	OMe	H	H	CSSMe	Me	Me
I-78	OMe	H	H	OMe	H	CSSMe	Me	Me
I-79	OMe	H	OMe		H	CSSMe	Me	Me
I-80	H	$-OCH_2O-$		H	H	CSSMe	Me	Me
I-81	Pr^i	H	NO_2	H	H	CSSMe	Me	Me
I-82	Pr^i	H	H	H	NO_2	CSSMe	Me	Me
I-83	H	OMe	OMe	OMe	H	CSSMe	Me	Me
I-84	Pr^i	H	H	H	H	CSSEt	Me	Me
I-85	Bu^s	H	H	H	H	CSSEt	Me	Me
I-86	OEt	H	H	H	H	CSSEt	Me	Me
I-87	SMe	H	H	H	H	CSSEt	Me	Me
I-88	H	Pr^i	H	H	H	CSSEt	Me	Me
I-118	H	OEt	OEt	H	H	CSSMe	Me	Me
I-119	OMe	H	Me	H	H	CSSMe	Me	Me
I-120	OMe	H	H	Me	H	CSSMe	Me	Me
I-121	H	OMe	Me	H	H	CSSMe	Me	Me
I-122	Me	Me	H	H	H	CSSMe	Me	Me
I-123	N(Me)Ac	H	H	H	H	CSSMe	Me	Me

(Table 4)



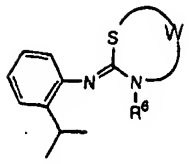
	R^6	R^7	R^8
I-89	COPr	Me	Me
I-90	COOMe	Me	Me
I-91	COOPr	Me	Me
I-92	CONHEt	Me	Me
I-93	$COCH_2OMe$	Me	Me
I-94	$COCH_2SMe$	Me	Me
I-95	$COCH_2SEt$	Me	Me
I-96	CSOEt	Me	Me
I-97	CSNHEt	Me	Me
I-98	CSSPr	Me	Me
I-99	CSSPr'	Me	Me
I-100	CSSBn	Me	Me

(Table 5)



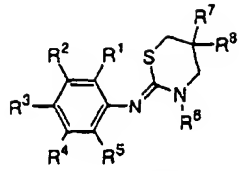
	R^1	R^2	R^3	n	R^6	R^7	R^8
I-101	H	H	Cl	1	COSEt	Me	Me
I-102	H	H	Cl	1	CSSMe	Me	Me
I-103	Cl	H	Cl	2	COSEt	Me	Me
I-104	Cl	H	Cl	2	CSSMe	Me	Me

(Table 6)



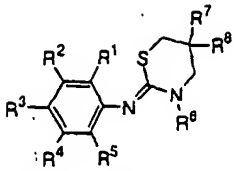
	R^6	W
I-105	COSEt	
I-106	COSEt	
I-107	COSEt	
I-108	COSEt	
I-109	COSEt	
I-110	COSEt	
I-111	COSEt	
I-112	COSEt	
I-113	CSSMe	
I-114	CSSMe	
I-115	CSSMe	
I-116	CSSMe	
I-117	CSSMe	

(Table 7)



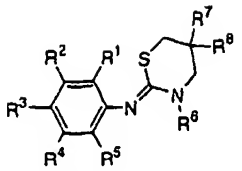
	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
I-124	H	H	OEt	H	H	CSSMe	Me	Me
I-125	H	OEt	H	H	H	CSSMe	Me	Me
I-126	H	H	OMe	H	H	CSSMe	Me	Me
I-127	H	OMe	H	H	H	CSSMe	Me	Me
I-128	H	OEt	OMe	H	H	CSSMe	Me	Me
I-129	H	OPr	OMe	H	H	CSSMe	Me	Me
I-130	H	OEt	OEt	H	H	CSSMe	Me	Me
I-131	H	H	OPr	H	H	CSSMe	Me	Me
I-132	H	OPr	H	H	H	CSSMe	Me	Me
I-133	H	H	OBu	H	H	CSSMe	Me	Me
I-134	H	OBu	H	H	H	CSSMe	Me	Me
I-135	H	OMe	OEt	H	H	CSSMe	Me	Me
I-136	H	OMe	OPr	H	H	CSSMe	Me	Me
I-137	H	OBu	OMe	H	H	CSSMe	Me	Me
I-138	H	H	OPr^i	H	H	CSSMe	Me	Me
I-139	H	OPr^i	H	H	H	CSSMe	Me	Me
I-140	H	H	H	H	H	CSSMe	Me	Me
I-141	F	H	H	H	H	CSSMe	Me	Me
I-142	Cl	H	H	H	H	CSSMe	Me	Me
I-143	H	Cl	H	H	H	CSSMe	Me	Me
I-144	Me	H	H	H	H	CSSMe	Me	Me
I-145	H	Me	H	H	H	CSSMe	Me	Me
I-146	H	H	Me	H	H	CSSMe	Me	Me
I-147	H	Bu	H	H	H	CSSMe	Me	Me
I-148	H	H	Bu	H	H	CSSMe	Me	Me

(Table 8)



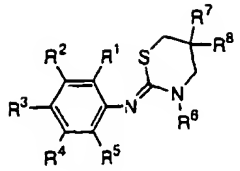
	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
I-149	Bu^t	H	H	H	H	CSSMe	Me	Me
I-150	H	H	Et	H	H	CSSMe	Me	Me
I-151	H	Et	H	H	H	CSSMe	Me	Me
I-152	H	H	F	H	H	CSSMe	Me	Me
I-153	H	F	H	H	H	CSSMe	Me	Me
I-154	H	H	Pr^i	H	H	CSSMe	Me	Me
I-155	H	H	Morpho lino	H	H	CSSMe	Me	Me
I-156	H	Ac	H	H	H	CSSMe	Me	Me
I-157	H	H	Br	H	H	CSSMe	Me	Me
I-158	H	Br	H	H	H	CSSMe	Me	Me
I-159	Br	H	H	H	H	CSSMe	Me	Me
I-160	H	C(Me)= NOMe	H	H	H	CSSMe	Me	Me
I-161	H	H	Ac	H	H	CSSMe	Me	Me
I-162	H	H	C(Me)= NOMe	H	H	CSSMe	Me	Me
I-163	OPr^i	H	H	H	H	CSSMe	Me	Me
I-164	Pr	H	H	H	H	CSSMe	Me	Me
I-165	CF_3	H	H	H	H	CSSMe	Me	Me
I-166	H	H	OPh	H	H	CSSMe	Me	Me
I-167	H	H	Pr	H	H	CSSMe	Me	Me
I-168	H	H	Bu^t	H	H	CSSMe	Me	Me
I-169	H	CF_3	H	H	H	CSSMe	Me	Me
I-170	H	H	CF_3	H	H	CSSMe	Me	Me
I-171	Pr^i	H	NHAc	H	H	CSSMe	Me	Me
I-172	Pr^i	H	H	H	NHAc	CSSMe	Me	Me
I-173	H	COOMe	H	H	OMe	CSSMe	Me	Me

(Table 9)



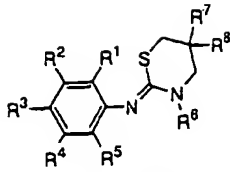
	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
I-174	Morpholino	H	H	H	H	CSSMe	Me	Me
I-175	H	Morpholino	H	H	H	CSSMe	Me	Me
I-176	Pr^i	H	H	COOEt	H	CSSMe	Me	Me
I-177	H	H	Piperidino	H	H	CSSMe	Me	Me
I-178	Pyrrolidino	H	H	H	H	CSSMe	Me	Me
I-179	H	SMe	H	H	H	CSSMe	Me	Me
I-180	H	H	SMe	H	H	CSSMe	Me	Me
I-181	OCF_3	H	H	H	H	CSSMe	Me	Me
I-182	H	OCF_3	H	H	H	CSSMe	Me	Me
I-183	H	H	OCF_3	H	H	CSSMe	Me	Me
I-184	H	H	3-Pyridyl	H	H	CSSMe	Me	Me
I-185	H	3-Pyridyl	H	H	H	CSSMe	Me	Me
I-186	3-Pyridyl	H	H	H	H	CSSMe	Me	Me
I-187	OPh	H	H	H	H	CSSMe	Me	Me
I-188	H	OEt	OEt	H	H	COOMe	Me	Me
I-189	OMe	H	H	H	H	COOMe	Me	Me
I-190	H	H	Et	H	H	COOMe	Me	Me
I-191	H	H	Pr^i	H	H	COOMe	Me	Me
I-192	OMe	H	H	H	H	COSMe	Me	Me
I-193	H	H	Et	H	H	COSMe	Me	Me
I-194	H	H	Pr^i	H	H	COSMe	Me	Me
I-195	H	H	OEt	H	H	COSMe	Me	Me
I-196	H	OMe	OEt	H	H	COSMe	Me	Me
I-197	H	Piperidino	H	H	H	CSSMe	Me	Me
I-198	H	H	NEt_2	H	H	CSSMe	Me	Me

(Table 10)



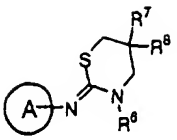
	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
I-199	OMe	H	COOMe	H	H	CSSMe	Me	Me
I-200	H	2-Oxopyrrolidino	H	H	H	CSSMe	Me	Me
I-201	H	OPh	H	H	H	CSSMe	Me	Me
I-202	H	H	Ph	H	H	CSSMe	Me	Me
I-203	Ph	H	H	H	H	CSSMe	Me	Me
I-204	H	Ph	H	H	H	CSSMe	Me	Me
I-205	Pr^i	H	H	H	H	CSOMe	Me	Me
I-206	Pr^i	H	I	H	H	CSSMe	Me	Me
I-207	OMe	H	(Morpholino)CO	H	H	CSSMe	Me	Me
I-208	H	H	NMe_2	H	H	CSSMe	Me	Me
I-209	H	NMe_2	H	H	H	CSSMe	Me	Me
I-210	N(Me)Et	H	H	H	H	CSSMe	Me	Me
I-211	N(Me)Pr	H	H	H	H	CSSMe	Me	Me
I-212	NEt_2	H	H	H	H	CSSMe	Me	Me
I-213	F	H	H	H	F	CSSMe	Me	Me
I-214	Pr^i	H	Cl	H	H	CSSMe	Me	Me
I-215	NMe_2	Me	H	H	H	CSSMe	Me	Me
I-216	NMe_2	H	Me	H	H	CSSMe	Me	Me
I-217	NMe_2	H	H	Me	H	CSSMe	Me	Me
I-218	NMe_2	H	H	Cl	H	CSSMe	Me	Me
I-219	Me	H	H	H	Me	CSSMe	Me	Me
I-220	NMe_2	H	H	H	H	CSSEt	Me	Me
I-221	H	NMe_2	H	H	H	CSSEt	Me	Me
I-222	NMe_2	H	Me	H	H	CSSEt	Me	Me
I-223	H	H	Pr^i	H	H	CSSEt	Me	Me

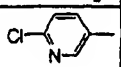
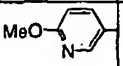
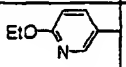
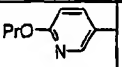
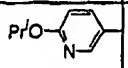
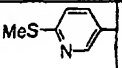
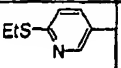
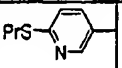
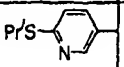
(Table 11)



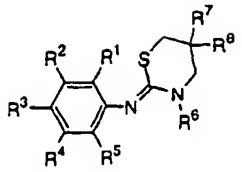
	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
I-224	OMe	H	CONHMe	H	H	CSSMe	Me	Me
I-225	$OCHF_2$	H	H	H	H	CSSMe	Me	Me
I-226	H	$OCHF_2$	H	H	H	CSSMe	Me	Me
I-227	H	NEt_2	H	H	H	CSSMe	Me	Me
I-228	NMe_2	H	Cl	H	H	CSSMe	Me	Me
I-229	NMe_2	H	F	H	H	CSSMe	Me	Me
I-230	NMe_2	H	H	F	H	CSSMe	Me	Me
I-231	NMe_2	H	Et	H	H	CSSMe	Me	Me
I-232	NMe_2	H	H	Et	H	CSSMe	Me	Me
I-233	NMe_2	H	Cl	H	H	CSSEt	Me	Me
I-234	NMe_2	H	F	H	H	CSSEt	Me	Me
I-235	NMe_2	H	Et	H	H	CSSEt	Me	Me
I-236	Pr^i	H	H	H	H	$CSSBu^s$	Me	Me
I-237	Pr^i	H	H	H	H	$CSSBu^t$	Me	Me
I-238	Pr^i	H	H	H	H	CSNHMe	Me	Me
I-239	Me	NMe_2	H	H	H	CSSMe	Me	Me
I-240	NMe_2	OMe	H	H	H	CSSMe	Me	Me
I-241	H	NMe_2	Me	H	H	CSSMe	Me	Me
I-242	NMe_2	Cl	H	H	H	CSSMe	Me	Me
I-243	H	NMe_2	OMe	H	H	CSSMe	Me	Me
I-244	Pr^i	H	H	H	H	CSSEt	Et	Et
I-245	Pr^i	H	H	H	H	Me	Me	Me
I-246	Pr^i	H	H	H	H	Pr	Me	Me
I-247	Pr^i	H	H	H	H	Pr^i	Me	Me
I-248	Pr^i	H	H	H	H	Bu^t	Me	Me

(Table 12)



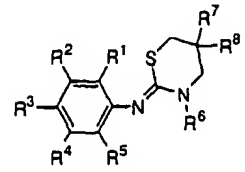
	A	R^6	R^7	R^8
I-249		CSSMe	Me	Me
I-250		CSSMe	Me	Me
I-251		CSSMe	Me	Me
I-252		CSSMe	Me	Me
I-253		CSSMe	Me	Me
I-254		CSSMe	Me	Me
I-255		CSSMe	Me	Me
I-256		CSSMe	Me	Me
I-257		CSSMe	Me	Me
I-258		CSSMe	Me	Me
I-259		CSSMe	Me	Me
I-260		CSSMe	Me	Me
I-261		CSSMe	Me	Me

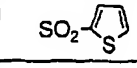
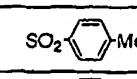
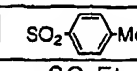
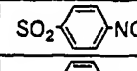
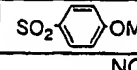
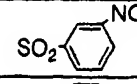
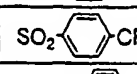
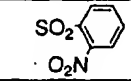
(Table 13)



	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
I-262	NMe_2	H	OMe	H	H	CSSMe	Me	Me
I-263	NMe_2	H	H	OMe	H	CSSMe	Me	Me
I-264	Me	NEt_2	H	H	H	CSSMe	Me	Me
I-265	H	NEt_2	Me	H	H	CSSMe	Me	Me
I-266	H	NEt_2	OMe	H	H	CSSMe	Me	Me
I-267	Bu^s	H	H	H	H	CSSMe	Et	Et
I-268	Pr^i	H	H	H	H	CSSMe	Pr	Pr
I-269	Pr^i	H	H	H	H	CSSMe	$-(CH_2)_4-$	
I-270	Pr^i	H	H	H	H	CSSMe	$-(CH_2)_5-$	

(Table 14)



	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
I-271	Pr^i	H	H	H	H	SO_2Me	Me	Me
I-272	Pr^i	H	H	H	H		Me	Me
I-273	Pr^i	H	H	H	H		Me	Me
I-274	H	Pr^i	H	H	H		Me	Me
I-275	H	Pr^i	H	H	H	SO_2Et	Me	Me
I-276	H	Pr^i	H	H	H		Me	Me
I-277	H	Pr^i	H	H	H		Me	Me
I-278	H	Pr^i	H	H	H		Me	Me
I-279	H	Pr^i	H	H	H		Me	Me
I-280	H	Pr^i	H	H	H		Me	Me

[0141] Physical Date (M.p., ^{1}H-NMR) of the compounds in the above Tables are shown in the following Tables.

(Table 15)

Comp. No.	Physical Date	
No	M.p.	
I-16	57-59°C	1.16 (6H, s), 1.31 (3H, t, J = 7.3), 2.64 (2H, s), 2.91 (2H, q, J = 7.3), 3.78 (2H, s), 6.96 (1H,dd, J = 7.4, 1.2), 7.14 (1H, t, J = 7.4), 7.36 (2H, t, J = 7.4).
I-17		1.15 (6H, s), 1.31 (3H, t, J = 7.3), 2.67 (2H, s), 2.91 (2H, q J = 7.3), 3.77 (2H, s), 7.10-7.15 (4H, m).
I-18		1.16 (6H, s), 1.31 (3H, t, J = 7.3), 2.68 (2H, s), 2.92 (2H, q, J = 7.3), 3.80 (2H, s), 6.96 (1H, dd, J = 7.7, 1.2), 7.08 (1H, dt, J = 7.7, 1.6), 7.25 (2H, t, J = 7.4), 7.40 (1H, d, J = 7.4).
I-19		1.15 (6H, s), 1.27 (3H, t, J = 7.3), 2.24 (3H, s), 2.62 (2H, s), 2.92 (2H, q, J = 7.4), 3.77 (2H, s), 6.83 (1H, d, J = 7.7), 7.04 (1H, t, J = 7.7), 7.16-7.22 (2H, m).
I-20		1.15 (6H, s), 1.19 (3H, t, J = 7.4), 1.31 (3H, t, J = 7.3), 2.62 (2H, q, J = 7.3), 2.65 (2H, s), 2.94 (2H, q, J = 7.4), 3.77 (2H, s), 6.83 (1H, d, J = 7.6), 7.10-7.22 (3H, m).
I-21		0.95 (3H, t, J = 7.3), 1.15 (6H, s), 1.30 (3H, t, J = 7.4), 1.50-1.64 (2H, m), 2.56 (2H, q, J = 7.3), 2.59 (2H, s), 2.90 (2H, q, J = 7.4), 3.76 (2H, s), 6.82 (1H, d, J = 7.3), 7.06-7.28 (3H, m).
I-22		0.90 (3H, t, J = 7.1), 1.15 (6H, s), 1.29 (3H, t, J = 7.4), 1.30-1.34 (2H, m), 1.52-1.58 (2H, m), 2.54 (2H, q, J = 7.1), 2.62 (2H, s), 2.92 (2H, q, J = 7.4), 3.76 (2H, s), 6.79 (1H, dd, J = 7.9, 1.4), 7.06-7.28 (3H, m).
I-23		0.86 (3H, t, J = 7.4), 1.14 (6H, s), 1.16 (6H, d, J = 6.9), 1.29 (3H, t, J= 7.4), 1.48-1.58 (2H, m), 2.61 (2H, s), 2.89 (2H, q, J = 7.4), 2.88-2.92 (1H, m), 3.76 (2H, d, J = 13.6), 3.82 (1H, d, J = 13.6), 6.82-6.88 (1H, m), 7.10-7.18 (1H, m), 7.23-7.29 (1H, m).
I-24		1.15 (6H, s), 1.27 (3H, t, J = 7.4), 1.33 (9H, s), 2.68 (2H, s), 2.86 (2H, q, J = 7.4), 3.75 (2H, s), 6.86 (1H, dd, J = 7.4, 1.6), 7.08-7.19 (2H, m), 7.38 (2H, dd, J = 7.4, 1.6).
I-25		0.99 (6H, s), 1.25 (3H, t, J = 7.4), 2.45 (2H, s), 2.82 (2H, q, J = 7.4), 3.51 (2H, s), 6.98 (1H, d, J = 7.7), 7.20-7.36 (6H, m), 7.43 (2H, m).
I-26	82-83°C	1.15 (6H, s), 1.29 (3H, t, J = 7.3), 2.66 (2H, s), 2.89 (2H, q, J = 7.4), 3.77 (2H, s), 6.98 (1H, d, J = 7.6), 7.19 (1H, t, J = 7.6), 7.49 (1H, t, J = 7.6), 7.64 (1H, d, J = 7.6).

(Table 16)

Comp. No.	Physical Date	
No	M.p.	
I-27		1.16 (6H, s), 1.25 (3H, t, J = 7.4), 2.62 (2H, s), 2.88 (2H, q, J = 7.4), 3.78 (2H, s), 3.83 (3H, s), 6.91-6.96 (3H, m), 7.05-7.14 (1H, m).
I-28		1.15 (6H, s), 1.30 (3H, t, J = 7.4), 1.40 (3H, t, J = 7.0), 2.60 (2H, s), 2.90 (2H, q, J = 7.4), 3.78 (2H, s), 4.08 (2H, q, J = 7.0), 6.90-6.94 (3H, m), 7.06-7.08 (1H, m).
I-29		1.14 (6H, s), 1.29 (6H, d, J =7.4), 1.31 (6H, d, J = 6.0), 2.59 (2H, s), 2.89 (2H, q, J = 7.4), 3.76 (2H, s), 4.50 (1H, q, J = 6.0), 6.90-6.93 (3H, m), 7.01-7.07 (1H, m).
I-30	78-80°C	1.15 (6H, s), 1.29 (3H, t, J = 7.4), 2.43 (3H, s), 2.63 (2H, s), 2.89 (2H, q, J = 7.4), 3.78 (2H, s), 6.87-6.91 (1H, m), 7.05-7.14 (2H, m), 7.20-7.29 (1H, m).
I-31	55-57°C	1.15 (6H, s), 1.29 (3H, t, J = 7.4), 1.31 (3H, t, J = 7.4), 2.66 (2H, s), 2.89 (2H, q, J = 7.4), 2.94 (2H, q, J = 7.4), 3.78 (2H, s), 6.91 (1H, dd, J = 7.4, 1.6), 7.08-7.20 (2H, m), 7.32 (1H, dd, J = 7.4, 1.6).
I-32		1.15 (6H, s), 1.27 (6H, d, J =6.6), 1.28 (6H, d, J = 7.4), 2.65 (2H, s), 2.88 (2H, q, J = 7.4), 3.38-3.42 (1H, m), 3.78 (2H, s), 6.90 (1H, dd, J = 7.7, 1.6), 7.08-7.20 (2H, m), 7.32 (1H, dd, J = 7.7, 1.6).

(Table 16) (continued)

Comp. No.	Physical Date	
No	M.p.	
I-33		1.15 (6H, s), 1.29 (3H, t, J = 7.4), 2.60 (2H, s), 2.71 (6H, s), 2.89 (2H, q, J = 7.4), 3.77 (2H, s), 6.90-6.98 (3H, m), 7.05-7.10 (1H, m).
I-34		1.16 (6H, s), 1.27 (6H, d, J = 6.9), 1.31 (3H, t, J = 7.4), 2.64 (2H, s), 2.91 (2H, q, J = 7.4), 2.98 (1H, q, J = 6.9), 3.77 (2H, s), 6.78-6.83 (2H, m), 7.01-7.04 (1H, m), 7.25-7.27 (1H, m).
I-35	68-69°C	1.16 (6H, s), 1.30 (3H, t, J = 7.3), 2.66 (2H, s), 2.90 (2H, q, J = 7.3), 3.76 (2H, s) 6.98 (2H, dd, J = 6.6, 2.1), 7.31 (2H, dd, J = 6.6, 2.1).
I-36	67-69°C	1.15 (6H, s), 1.20 (6H, d, J = 6.9), 1.26 (3H, t, J = 7.4), 2.64 (2H, s), 2.86 (2H, q, J = 7.4), 2.89 (1H, q, J = 6.9), 3.75 (2H, s), 6.98 (2H, d, J = 8.2), 7.20 (2H, d, J = 8.3).
I-37	125-126°C	1.15 (6H, s), 1.30 (3H, t, J = 7.3), 2.72 (2H, s), 2.92 (2H, q, J = 7.3), 3.78 (2H, s), 7.05 (2H, d, J =8.3), 7.31 (2H, d, J = 8.3).
I-38	76-78°C	1.15 (6H, s), 1.30 (3H, t, J = 7.4), 2.14 (3H, s), 2.29 (3H, s), 2.63 (2H, s), 2.89 (2H, q, J = 7.4), 3.77 (2H, s), 6.70 (1H, d, J = 7.9), 6.94 (1H, d, J = 7.9), 7.06 (1H, s).

(Table 17)

Comp. No.	Physical Date	
No	M.p.	
I-39		1.14 (6H, s), 1.29 (3H, t, J = 7.4), 2.21 (3H, s), 2.32 (3H, s), 2.65 (2H, s), 2.89 (2H, q, J = 7.4), 3.76 (2H, s), 6.73 (1H, d, J = 7.9), 6.97 (1H, d, J = 7.9), 7.02 (1H, s).
I-40		1.15 (6H, s), 1.30 (3H, t, J = 7.4), 2.19 (3H, s), 2.31 (3H, s), 2.64 (2H, s), 2.89 (2H, q, J = 7.4), 3.77 (2H, s), 6.65 (1H, s), 6.86 (1H, d, J = 7.9), 7.07 (1H, d, J = 7.7).
I-41	59-61°C	1.15 (6H, s), 1.30 (3H, t, J = 7.3), 2.19 (6H, s), 2.62 (2H, s), 2.90 (2H, q, J = 7.3), 3.78 (2H, s), 6.90-6.96 (1H,m), 7.02-7.08 (2H, m).
I-42		1.15 (6H, s), 1.31 (3H, t, J = 7.4), 2.26 (3H, s), 2.28 (3H, s), 2.65 (2H, s), 2.91 (2H, q, J = 7.4), 3.78 (2H, s), 6.74 (1H, dd, J = 7.9, 1.8), 6.80 (1H, d, J = 1.8), 7.13 (1H, d, J = 7.7).
I-43		1.15 (6H, s), 1.31 (3H, t, J = 7.4), 2.31 (6H, s), 2.63 (2H, s), 2.90 (2H, q, J = 7.4), 3.76 (2H, s), 6.58 (2H, s), 6.77 (1H, s).
I-44		1.15 (6H, s), 1.28 (3H, t, J = 7.4), 2.21 (3H, s), 2.64 (2H, s), 2.90 (2H, q, J = 7.4), 3.76 (2H, s), 6.74 (1H, d, J = 8.2), 7.10-7.18 (2H, m).
I-45		1.15 (6H, s), 1.28 (3H, t, J = 7.4), 2.31 (3H, s), 2.66 (2H, s), 2.92 (2H, q, J = 7.4), 3.78 (2H, s), 6.74 (1H, d, J = 7.8), 7.04 (1H, d, J = 7.8), 7.25 (1H, d, J = 7.8).
I-46	119-120°C	1.16 (6H, s), 1.25 (6H, d, J = 6.9), 1.29 (3H, t, J = 7.4), 2.69 (2H, s), 2.90 (2H, q, J = 7.4), 3.15 (1H, m), 3.79 (2H, s), 6.92 (1H, d, J = 8.7), 8.01 (1H, dd, J = 8.5, 2.4), 8.18 (1H, d, J = 2.4).
I-47		1.17 (6H, s), 1.23 (6H, d, J = 6.9), 1.30 (3H, t, J = 7.4), 2.69 (2H, s), 2.91 (2H, q, J = 7.4), 3.19 (1H, m), 3.79 (2H, s), 7.41 (1H, d, J = 8.7), 7.71 (1H, d, J = 2.4), 7.92 (1H, dd, J = 8.7, 2.4).
I-48		1.15 (6H, s), 1.30 (3H, t, J = 7.4), 2.73 (2H, s), 2.93 (2H, q, J = 7.4), 3.82 (2H, s) 7.15 (2H, d, J =8.3), 8.48 (1H, dd, J = 8.3, 1,4), 8.90 (1H, d, J =8.3).
I-49	64-66°C	0.95 (3H, t, J = 7.3), 1.15 (6H, s), 1.50-1.64 (2H, m), 2.32 (3H, s), 2.56 (2H, q, J = 7.3), 2.63 (2H, s),3.78 (2H, s), 6.82 (1H, d, J = 7.3), 7.06-7.28 (3H, m).
I-50	95-96°C	1.16 (6H, s), 1.20 (6H, d, J = 6.9), 2.32 (3H, s), 2.64 (2H, s), 3.12 (1H, q, J = 6.9), 3.79 (2H, s), 6.78-6.82 (1H, m), 7.11-7.20 (2H, m), 7.30-7.34 (1H, m).

(Table 18)

Comp . No.	Physical Date	
No	M.p.	
I-51	53-56°C	0.85 (3H, t, J = 7.3), 1.15 (6H, d, J = 6.9), 1.18 (6H, s), 1.57-1.70 (2H, m), 2.31 (3H, s), 2.62 (2H, s), 2.91 (1H, q, J = 6.9), 3.74 (1H, d, J = 13.7), 3.78 (1H, d, J = 13.7), 6.78-6.83 (1H, m), 7.11-7.18 (2H, m), 7.23-7.30 (1H, m).
I-52	88-90°C	1.17 (6H, s), 1.27 (6H, d, J = 6.9), 2.33 (3H, s), 2.65 (2H, s), 2.91 (1H, q, J = 6.9), 3.79 (2H, s), 6.78-6.83 (2H, m), 7.01-7.04 (1H, m), 7.20-7.24 (1H, m).
I-53		1.16 (6H, s), 2.32 (3H, s), 2.65 (2H, s), 3.77 (2H, s), 3.87 (6H, s), 6.51-6.59 (2H, m), 6.80-6.89 (1H, m).
I-54	102-104°C	1.15 (6H, s), 2.31 (3H, s), 2.65 (2H, s), 3.76 (2H, s), 5.96 (2H, s), 6.42 (1H, dd, J = 8.1, 1.8), 6.53 (1H, d, J = 1.8), 6.78 (1H, d, J = 8.1).
I-55	129-131°C	1.16 (6H, s), 2.32 (3H, s), 2.67 (2H, s), 3.78 (2H, s), 3.85 (6H, s), 3.86 (3H, s), 6.20 (2H, s)
I-56	107-109°C	1.17 (3H, t, J = 7.6), 1.22 (6H, s), 2.58 (2H, q, J = 7.6), 2.64 (3H, s), 2.66 (2H, s), 4.51 (2H, s), 6.91 (1H, dd, J = 7.5, 1.3), 7.02-7.19 (2H, m), 7.23-7.28 (1H, m).
I-57		0.85 (3H, t, J = 7.3), 1.18 (6H, d, J = 6.9), 1.23 (6H, s), 1.57-1.70 (2H, m), 2.64 (3H, s), 2.66 (2H, s), 2.88 (1H, q, J = 6.9), 4.38 (1H, d, J = 13.7), 4.60 (1H, d, J = 13.7), 6.83-6.90 (1H, m), 7.11-7.18 (2H, m), 7.28-7.35 (1H, m).
I-58	85-87°C	1.22 (6H, s), 2.62 (3H, s), 2.63 (2H, s), 3.35 (3H, s), 4.40 (2H, s), 4.48 (2H, s), 6.93-6.99 (1H, m), 7.11-7.29 (2H, m), 7.40-7.49 (1H, m).
I-59	113-114°C	1.22 (3H, s), 1.24 (3H, s), 1.37 (3H, d, J = 6.4), 2.63 (3H, s), 2.65 (2H, s), 3.24 (3H, s), 4.35 (1H, d, J = 13.6), 4.55 (1H, q, J = 6.4), 4.66 (1H, d, J = 13.6), 6.91 (1H, d, J = 7.4), 7.19-7.40 (2H, m), 7.51 (1H, d, J = 7.4).
I-60	128-130°C	1.22 (6H, s), 2.62 (3H, s), 2.65 (2H, s), 3.85 (3H, s), 4.53 (2H, s), 6.93-6.99 (2H, m), 7.02-7.15 (2H, m).
I-61	100-101°C	1.26 (6H, s), 1.43 (3H, t, J = 7.4), 2.66 (2H, s), 2.67(3H,s), 4.08 (2H, q, J = 7.0), 4.55 (2H, s), 6.95-6.99 (3H, m), 7.11-7.18 (1H, m).
I-62	137-139°C	1.23 (6H, s), 2.43 (3H, s), 2.64 (3H,s), 2.67 (2H, s), 4.53 (2H, s), 6.87-6.92 (1H, m), 7.11-7.20 (2H, m), 7.23-7.29 (1H, m).

(Table 19)

Comp. No.	Physical Date	
No	M.p.	
I-63	103-105°C	1.15 (6H, s), 1.29 (3H, t, J = 7.4), 1.31 (3H, t, J = 7.4), 2.66 (2H, s), 2.89 (2H, q, J = 7.4), 2.94 (2H, q, J = 7.4), 3.78 (2H, s), 6.91 (1H, dd, J = 7.4, 1.6), 7.08-7.20 (2H, m), 7.32 (1H, dd, J = 7.4, 1.6).
I-64	125-126°C	1.24 (6H, s), 1.28 (6H, d, J =6.6), 2.63(3H, s), 2.66 (2H, s), 3.38-3.42 (1H, m), 4.53 (2H, s), 6.97 (1H, dd, J = 7.7, 1.6), 7.08-7.20 (2H, m), 7.32 (1H, dd, J = 7.7, 1.6).
I-65		1.22 (6H, s), 2.63 (3H, s), 2.65 (2H, d, J = 13.6), 2.75 (3H, s), 4.17 (1H, d, J = 13.6), 4.77 (1H, d, J = 13.6), 7.06 (1H, dd, J = 7.7, 1.7), 7.19-7.40 (2H, m), 7.97 (1H, dd, J = 7.7, 1.7).
I-66	147-149°C	1.23 (6H, s), 2.63 (3H, s), 2.71 (2H, s), 3.13 (3H, s), 4.52 (2H, s), 7.11 (1H, m,), 7.11-7.20 (2H, m), 7.23-7.29 (1H, m).

(Table 19) (continued)

Comp. No.	Physical Date	
No	M.p.	
I-67	129-130°C	1.22 (6H, s), 1.23 (3H, t, J = 6.9), 2.63 (3H, s), 2.66 (2H, s), 2.70-2.85 (1H, m), 2.90-3.15 (1H, m), 4.25 (1H, d, J = 13.6), 4.70 (1H, d, J = 13.6), 7.06 (1H, d, J = 7.5), 7.30-7.45 (2H, m), 7.90 (1H, d, J = 7.5).
I-68	100-102°C	1.23 (6H, s), 2.62 (3H, s), 2.65 (2H, s), 2.71 (6H, s), 4.50 (2H, s), 6.93-6.99 (3H, m), 7.02-7.15 (1H, m).
I-69		1.23 (6H, s), 1.25 (6H, d, J = 6.9), 2.64 (3H, s), 2.66 (2H, s), 2.92 (1H, q, J = 6.9), 4.52 (2H, s), 6.84-6.86 (2H, m), 7.08-7.13 (1H, m), 7.28-7.32 (1H, m).
I-70	116-118°C	1.23 (6H, s), 2.64 (3H, s), 2.68 (2H, s), 4.51 (2H, s), 6.97 (2H, d, J = 8.6), 7.35 (2H, d, J = 8.6).
I-71	103-105°C	1.22 (6H, s), 2.19 (3H, s), 2.30 (3H, s), 2.63 (3H, s), 2.65 (2H, s), 4.50 (2H, s), 6.79 (1H, d, J = 7.9), 6.98 (1H, d, J = 7.9), 7.02 (1H, s).
I-72	100-101°C	1.23 (6H, s), 2.18 (3H, s), 2.32 (3H, s), 2.64 (3H, s), 2.65 (2H, s), 4.51 (2H, s), 6.71 (1H, s), 6.88 (1H, d, J = 7.9), 7.08 (1H, t, J = 7.9).
I-73	93-95°C	1.22 (6H, s), 2.12 (3H, s), 2.30 (3H, s), 2.64 (3H, s), 2.65 (2H, s), 4.51 (2H, s), 6.76 (1H, d, J = 7.9), 6.98 (1H, d, J = 7.9), 7.08 (1H, t, J = 7.9).
I-74	126-128°C	1.23 (6H, s), 2.25 (3H, s), 2.27 (3H, s), 2.64 (3H, s), 2.65 (2H, s), 4.51 (2H, s), 6.76 (1H, d, J = 7.9), 6.82 (1H, s), 713 (1H, d, J = 7.9).
I-75	96-98°C	1.23 (6H, s), 2.32 (6H, s), 2.63 (3H, s), 2.65 (2H, s), 4.51 (2H, s), 6.64 (2H, s), 6.80 (1H,s).
I-76		1.22 (6H, s), 2.64 (3H, s), 2.65 (2H, s), 3.79 (3H, s), 3.88 (3H, s), 4.52 (2H, s), 6.60 (1H, d, J = 7.9), 6.73 (1H, d, J = 7.9), 7.04 (1H, d, J = 7.9).

(Table 20)

Comp. No.	Physical Date	
No	M.p.	
I-77		1.24 (6H, s), 2.63 (3H, s), 2.68 (2H, s), 3.87 (6H, s), 4.50 (2H, s), 6.61-6.65 (2H, m), 6.85-6.89 (1H, m).
I-78		1.22 (6H, s), 2.62 (3H, s), 2.66 (2H, s), 3.81 (6H, s), 4.52 (2H, s), 6.48 (1H, dd, J =8.5, 2.4), 6.51 (1H, d, J = 2.4), 6.92 (1H, d, J = 8.5).
I-79		1.22 (6H, s), 2.62 (3H, s), 2.64 (2H, s), 3.77 (6H, s), 4.52 (2H, s), 6.56 (1H, d, J = 2.4), 6.68 (1H, dd, J =8.5, 2.4), 686 (1H, d, J = 8.5).
I-80	108-110°C	1.23 (6H, s), 2.63 (3H, s), 2.66 (2H, s), 4.49 (2H, s), 6.04 (2H, s), 6.50 (1H, dd, J = 8.1, 1.8), 6.61 (1H, d, J = 1.8), 6.83 (1H, d, J = 8.1).
I-81		1.23 (6H, s), 1.25 (6H, d, J = 6.9), 2.65 (3H, s), 2.71 (2H, s), 3.11 (1H, q, J = 6.9), 4.51 (2H, s), 7.02 (1H, d, J = 8.5), 8.04 (1H, dd, J = 8.5, 2.7), 8.21 (1H, d, J = 2.7).
I-82		1.21 (6H, s), 1.24 (6H, d, J = 6.9), 2.63 (3H, s), 2.66 (2H, s), 3.17 (1H, q, J = 6.9), 4.51 (2H, s), 7.45 (1H, d, J = 8.5), 7.80 (1H, d, J = 2.4), 7.99 (1H, dd, J = 8.5, 2.4).
I-83		1.24 (6H, s), 2.64 (3H, s), 2.68 (2H, s), 3.85 (6H, s), 3.86 (3H, s), 4.51 (2H, s), 6.28 (2H, s).
I-84	68-70°C	1.22 (6H, d, J = 6.9), 1.23 (6H, s), 1.35 (3H, t, J =7.4), 2.65 (2H, s), 3.11 (1H, q, J = 6.9), 3.25 (2H, q, J = 6.9), 4.48 (2H, s), 6.89-6.92 (1H, m), 7.14-7.20 (2H, m), 7.30-7.34 (1H, m).

(Table 20) (continued)

Comp. No.	Physical Date	
No	M.p.	
I-85		0.85 (3H, t, J =7.4), 1.18 (6H, d, J = 6.9), 1.23 (6H, s), 1.35 (3H, t, J =7.4), 1.57-1.70 (2H, m), 2.56 (2H, s), 2.87 (1H, q, J = 6.9), 3.25 (2H, q, J = 7.4), 4.35 (1H, d, J = 13.7), 4.60 (1H, d, J = 13.7), 6.89-6.92 (1H, m), 7.10-7.18 (2H, m), 7.30-7.34 (1H, m).
I-86	96-97°C	1.23 (6H, s), 1.36 (3H, t, J = 7.0), 1.40 (3H, t, J = 7.0), 2.63 (2H, s), 3.27 (2H, q, J = 7.4), 4.06 (2H, q, J = 7.0), 4.51 (2H, s), 6.92-7.08 (3H, m), 7.11-7.15 (1H, m).
I-87	105-106°C	1.22 (6H, s), 1.35 (3H, t, J = 7.4), 2.43 (3H, s), 2.66 (2H, s), 3.26 (2H, q, J = 7.4), 4.50 (2H, s), 6.95-6.98 (1H, m), 7.10-7.17 (2H, m), 7.24-7.29 (1H, m).

(Table 21)

Comp . No.	Physical Date	
No	M.p.	
I-88		1.23 (6H, s), 1.25 (6H, d, J = 6.9), 1.35 (3H, t, J =7.4), 2.66 (2H, s), 2.90 (1H, q, J = 6.9), 3.28 (2H, q, J = 7.4), 4.50 (2H, s), 6.84-6.88 (2H, m), 7.08-7.13 (1H, m), 7.28-7.32 (1H, m).
I-89		0.98 (3H,t, J = 7.4), 1.12 (6H, s), 1.22 (6H, d, J = 6.9), 1.72-1.80 (2H,m), 2.58 (2H, s), 2.90 (2H, t, J = 7.4), 3.06 (1H, q, J = 6.9), 3.71 (2H, s), 6.71-6.76 (1H, m), 7.11-7.20 (2H, m), 7.30-7.34 (1H, m).
I-90	99-101°C	1.14 (6H, s), 1.21 (6H, d, J = 6.9), 2.58 (2H, s), 3.14 (1H, q, J = 6.9), 3.64 (2H, s), 3.86 (3H, s), 6.73-6.78 (1H, m), 7.11-7.18 (2H, m), 7.28-7.35 (1H, m).
I-91		1.00 (3H, t, J = 7.3), 1.14 (6H, s), 1.20 (6H, d, J = 6.9), 1.74 (2H, q, J = 7.3), 2.58 (2H, s), 3.16 (1H, q, J = 6.9), 3.65 (2H, s), 4.23 (2H, q, J = 6.9), 6.73-6.80 (1H, m), 7.12-7.18 (2H, m), 7.31-7.34 (1H, m).
I-92	52-53°C	1.13 (6H, s), 1.19 (6H, d, J = 6.9), 1.20 (3H, t, J = 7.4), 2.60 (2H, s), 2.98 (1H, q, J = 6.9), 3.38 (2H, q, J = 7.4), 3.77 (2H, s), 6.73-6.78 (1H, m), 7.09-7.18 (2H, m), 7.28-7.32 (1H, m).
I-93	76-78°C	1.14 (6H, s), 1.22 (6H, d, J = 6.9), 2.62 (2H, s), 2.96 (1H, q, J = 6.9), 3.48 (3H, s), 3.75 (2H, s), 4.64 (2H, s), 6.73-6.78 (1H, m), 7.10-7.17 (2H, m), 7.25-7.32 (1H, m).
I-94	61-62°C	1.14 (6H, s), 1.20 (6H, d, J = 6.9), 2.23 (3H, s), 2.68 (2H, s), 2.93 (1H, q, J = 6.9), 3.71 (2H, s), 3.94 (2H, s), 6.82-6.86 (1H, m), 7.10-7.18 (2H, m), 7.30-7.36 (1H, m).
I-95	50-52°C	1.13 (6H, s), 1.20 (6H, d, J = 6.9), 1.31 (3H, t, J = 7.3), 2.65 (2H, J = 7.3), 2.68 (2H, s), 2.90 (1H, q, J = 6.9), 3.71 (2H, s), 3.97 (2H, s), 6.82-6.86 (1H, m), 7.12-7.19 (2H, m), 7.30-7.36 (1H, m).
I-96	73-75°C	1.21 (6H, s), 1.22 (6H, d, J = 6.9), 1.42 (3H, t, J = 6.9), 2.61 (2H, s), 3.10 (1H, q, J = 6.9), 4.15 (2H, s), 4.65 (2H, q, J = 6.9), 6.74-6.78 (1H, m), 7.14-7.20 (2H, m), 7.30-7.34 (1H, m).
I-97	160-162°C	1.18 (6H, s), 1.22 (6H, d, J = 6.9), 1.25 (3H, t, J = 7.4), 2.60 (2H, s), 2.90 (1H, q, J = 6.9), 3.71 (2H, q, J = 7.4), 4.40 (2H, s), 6.74-6.78 (1H, m), 7.14-7.20 (2H, m), 7.30-7.34 (1H, m).
I-98		1.04 (3H, t, J = 7.4), 1.20 (6H, d, J = 6.9), 1.27 (6H, s), 1.73 (2H, m), 2.64 (2H, s), 3.12 (1H, q, J = 6.9), 3.22 (2H, t, J = 7.4), 4.48 (2H, s), 6.89-6.92 (1H, m), 7.10-7.20 (2H, m), 7.28-7.35 (1H, m).

(Table 22)

Comp. No.	Physical Date	
No	M.p.	
I-99	113-114°C	1.04 (6H, d, J =6.9), 1.27 (6H, s), 1.42 (3H, d, J = 6.9), 2.63 (2H, s), 3.14 (1H, q, J = 6.9), 4.02 (1H, q, J = 6.9), 4.46 (2H, s), 6.89-6.93 (1H, m), 7.10-7.20 (2H, m), 7.28-7.35 (1H, m).
I-100		1.10 (6H, d, J = 6.9), 1.22 (6H, s), 2.64 (2H, s), 3.08 (1H, q, J = 6.9), 4.48 (2H, s), 4.49 (2H, s), 6.83-6.90 (1H, m), 7.11-7.18 (2H, m), 7.20-7.38 (6H, m).
I-101		1.15 (6H, s), 1.25 (3H, t, J = 7.4), 2.70 (2H, s), 2.87 (2H, q, J = 7.4), 3.69 (2H, s), 4.55 (2H, s), 7.30-7.40 (4H, m).
I-102		1.24 (6H, s), 2.57 (3H, s), 2.73 (2H, s), 4.43 (2H, s), 4.58 (2H, s), 7.23-7.40 (4H, m).
I-103		1.11 (6H, s), 1.26 (3H, t, J = 7.4), 2.61 (2H, s), 2.83 (2H, q, J = 7.4), 3.10 (2H, t, J = 7.4), 3.65 (2H, s), 3.66 (2H, t, J = 7.4), 7.17 (1H, dd, J = 8.2, 2.1), 7.30 (1H, t, J = 8.2), 7.36 (1H, d, J = 2.1).
I-104		1.16 (6H, s), 2.55 (3H,s), 2.63 (2H, s), 3.13 (2H, t, J = 7.5), 3.69 (2H, t, J = 7.5), 4.35 (2H, s), 7.15 (1H, dd, J = 8.2, 2.1), 7.25 (1H, t, J = 8.2), 7.36 (1H, d, J = 2.1).
I-105		1.20 (6H, d, J = 6.9), 1.30 (3H, t, J = 7.4), 2.10-2.22 (2H, m), 2.88 (2H, t, J = 6.4), 2.94 (2H, q, J = 7.4), 3.11 (1H, q, J = 6.9), 4.05 (2H, t, J = 7.4), 6.82-6.86 (1H, m), 7.10-7.16 (2H, m), 7.28-7.34 (1H, m).
I-106		1.17-1.30 (12H, m), 1.45-1,52 (1H,m), 1.90-1.96 (1H, m), 2.92 (2H, q, J = 7.4), 2.95-3.05 (2H,m), 3.14-3.23 (1H,m), 3.72-3.75 (1H, m), 7.20-7.30 (2H,m), 7,40-7.45 (2H,m).
I-107		1.22 (6H, d, J = 6.9), 1.28 (3H, d, J = 6.6), 1.29 (3H, t, J = 7.4), 1.75-1.77 (1H,m), 2.29-2.34 (1H, m), 2.88 (2H, q, J = 7.4), 3.14 (1H, m), 3.31-3.36 (1H, m), 4.01-4.10 (2H, m), 6.81-6.85 (1H, m), 7.10-7.20 (2H, m), 7.28.7.35 (1H, m).
I-108		1.12 (3H,d, J = 6.6), 1.20 (6H, d, J = 6.9), 1.29 (3H, t, J = 7.4), 2.40-2.50 (1H, m), 2.57 (1H, dd, J = 13.5, 6.6), 2.91 (2H, q, J = 7.4), 2.95 (1H, m), 3.14 (1H, m), 3.45 (1H, dd, J = 13.5, 8.4), 4.30 (1H, dd, J = 13.5, 8.4), 6.81-6.85 (1H, m), 7.10-7.20 (2H, m), 7.28-7.35 (1H, m).

(Table 23)

Comp . No.	Physical Date	
No	M.p.	
I-109		0.88 (6H, t, J = 7.5), 1.22 (6H, d, J = 6.9), 1.29 (3H, t, J = 7.4), 1.45-1.52 (4H, m), 2.58 (2H, s), 2.89 (2H, q, J = 7.4), 3.15 (1H,m), 3.77 (2H, s), 6.78-6.83 (1H, m), 7.08-7.21 (2H, m), 7.30-7.35 (1H, m).
I-110	109-111°C	1.21 (6H, d, J = 6.9), 1.23 (6H, s), 1.25 (3H, t, J = 7.4), 2.81 (2H, q, J = 7.4), 2.90 (1H, t, J = 6.9), 3.05 (2H, s), 7.13-7.30 (2H, m), 7.36-7.45 (2H, m).
I-111		1.21 (6H, d, J = 6.9), 1.31 (3H, t, J = 7.4), 1.42 (3H, d, J = 6.7), 2.90 (2H, q, J = 7.4), 3.23 (1H, q, J = 6.9), 3.69 (1H, q, J = 6.6), 3.87-3.93 (1H, m), 6.78-6.82 (1H, m), 7.08-7.20 (2H, m), 7.25-7.30 (1H, m).
I-112		1.19-1.25 (9H, m), 1.14 (3H, d, J = 6.3), 2.76 (1H, d, J = 10.9), 2.96 (2H, t, J = 7.4), 3.22 (1H, q, J = 6.9), 3.44-3.48 (1H, m), 5.12 (1H, q, J = 6.3), 6.81-6.85 (1H, m), 7.09-7.16 (2H, m), 7.28-7.32 (1H, m).
I-113	126-128°C	1.18 (6H, d, J = 6.9), 1.22 (6H, d, J = 6.9), 1.45 (3H, t, J = 7.4), 1.80-1.91 (1H,m), 2.57-2.64 (2H, m), 2.61 (3H,s), 2.86-2.89 (1H, m), 3.07 (1H, m), 5.95-6.05 (1H, m), 6.98-7.00 (1H, m), 7.12-7.22 (2H, m), 7.28-7.35 (1H, m).

(Table 23) (continued)

Comp . No.	Physical Date	
No	M.p.	
I-114		1.20 (6H, d, J = 6.9), 1.28 (3H, d, J = 6.9), 1.82-1.88 (1H, m), 2.48-2.63 (1H, m), 2.63 (3H,s), 3.11 (1H, m), 3.29-3.35 (1H, m), 4.26(1H, m), 4.98 (1H, m), 6.90-6.95 (1H, m), 7.15-7.20 (2H, m), 7.30-7.35 (1H, m).
I-115		1.14 (3H, d, J = 6.5), 1.20 (6H, d, J = 6.9), 2.53 (1H, dd, J = 13.0, 5.4), 2.75 (3H,s), 2.80-2.85 (1H, m), 2.95 (1H, dd, J = 13.0, 5.4), 3.11 (1H, m), 3.72 (1H, dd, J = 13.0, 9.0), 5.15 (1H, dd, J = 13.0, 9.0), 6.90-6.95 (1H, m), 7.15-7.25 (2H, m), 7.30-7.35 (1H, m).
I-116	119-121°C	0.88 (6H, t, J = 7.5), 1.20 (6H, d, J = 6.9), 1.45-1.52 (4H, m), 2.62 (2H, s), 2.64 (3H, s), 3.15 (1H,m), 4.66 (2H, s), 6.78-6.83 (1H, m), 7.08-7.21 (2H, m), 7.30-7.35 (1H, m).
I-117	99-100°C	0.71-0.79 (1H, m), 0.85-0.90 (2H, m), 1.22 (6H, d, J = 6.9), 1.22-1.25 (1H, m), 2.61 (3H, s), 2.79 (3H, s), 3.00-3.05 (1H,m), 4.40 (2H, s), 6.92-6.95 (1H, m), 7.15-7.21 (2H, m), 7.30-7.35 (1H, m).

(Table 24)

Comp . No.	Physical Date	
No	M.p.	
I-118		1.23 (6H, s), 1.45 (6H, t, J = 7.4), 2.63 (3H, s), 2.67(2H,s), 4.08 (2H, q, J = 7.0), 4.55 (2H, s), 6.57-6.63 (2H, m), 6.85 (1H, d, J = 7.9).
I-119	116-118°C	1.24 (6H, s), 2.37 (3H, s), 2.64 (3H, s), 2.66 (2H, s), 3.84 (3H, s), 4.54 (2H, s), 6.75-6.80 (2H, m), 6.88 (1H, m).
I-120	92-93°C	1.23 (6H, s), 2.27 (3H, s), 2.63 (3H, s), 2.67 (2H, s), 3.84 (3H, s), 4.51 (2H, s), 6.51-6.58 (2H, m), 7.10 (1H, d, J = 7.9).
I-121	129-130°C	1.22 (6H, s), 2.30 (3H, s), 2.63 (3H, s), 2.65 (2H, s), 3.80 (3H, s), 4.53 (2H, s); 6.78-6.95 (3H, m).
I-122	93-95°C	1.22 (6H, s), 2.12 (3H, s), 2.30 (3H, s), 2.64 (3H, s), 2.65 (2H, s), 4.51 (2H, s), 6.76 (1H, d, J = 7.9), 6.98 (1H, d, J = 7.9), 7.08 (1H, t, J = 7.9).
I-123	151-152°C	1.22 (6H, s), 1.83 (3H, s), 2.63 (3H, s), 2.65 (2H, s), 3.17 (3H, s), 4.40 (1H, d, J = 13.6), 4.65 (1H, d, J = 13.6), 7.01 (1H, d, J = 7.9), 7.10-7.15 (2H, m), 7.30-7.35 (1H, m).

(Table 25)

Comp . No.	Physical Date	
No	M.p.	NMR($CHCl_3$)
I-124	105-106°C	1.23 (6H, s), 1.41 (3H, t, J=7.0), 2.63 (3H, s), 2.66 (2H, s), 4.08 (2H, q, J=7.0), 4.50 (2H, s), 6.88 (2H, d, J=8.6), 6.98 (2H, d, J=8.6).
I-125	92-94°C	1.23 (6H, s), 1.40 (3H, t, J=7.0), 2.62 (3H, s), 2.66 (2H, s), 4.08 (2H, q, J=7.0), 4.50 (2H, s), 6.57-6.63 (2H, m), 6.70-6.75 (1H, m), 7.25-7.30 (1H, m).
I-126	108-109°C	1.23 (6H, s), 2.63 (3H, s), 2.65 (2H, s), 3.81 (3H, s), 4.50 (2H, s), 6.92 (2H, d, J=8.6), 7.04 (2H, d, J=8.6).
I-127	62-64°C	1.23 (6H, s), 2.63 (3H, s), 2.66 (2H, s), 3.82 (3H, s), 4.50 (2H, s), 6.57-6.63 (2H, m), 6.70-6.75 (1H, m), 7.25-7.30 (1H, m).
I-128	78-79°C	1.23 (6H, s), 1.44 (3H, t, J=7.0), 2.59 (3H, s), 2.63 (2H, s), 3.82 (3H, s), 4.10 (2H, q, J=7.0), 4.47 (2H, s), 6.57-6.63 (2H, m), 6.82-6.87 (1H, m).

(Table 25) (continued)

Comp . No.	Physical Date	
No	M.p.	NMR($CHCl_3$)
I-129	58-60°C	1.04 (3H, t, J=7.0), 1.23 (6H, s), 2.00 (2H, sext, J= 7.0), 2.63 (3H, s), 2.67 (2H, s), 3.87 (3H, s), 4.10 (2H, t, J=7.0), 4.50 (2H, s), 6.58-6.64 (2H, m), 6.86-6.91 (1H, m).
I-130		1.13 (6H, s), 1.45 (6H, t, J=7.4), 2.28 (3H, s), 2.62 (2H, s), 3.74 (2H, s), 4.08 (4H, q, J=7.4), 6.46-6.53 (2H, m), 6.88-6.92 (1H, m).
I-131	91-93°C	1.04 (3H, t, J=7.0), 1.22 (6H, s), 1.76 (2H, sext, J=7.0), 2.63 (3H, s), 2.65 (2H, s), 3.91 (2H, t, J=7.0), 4.50 (2H, s), 6.90 (2H, d, J=8.6), 6.98 (2H, d, J = 8.6).
I-132	103-104°C	1.04 (3H, t, J = 7.0), 1.22 (6H, s), 1.76 (2H, sext, J = 7.0), 2.63 (3H, s), 2.65 (2H, s), 3.91 (2H, t, J=7.0), 4.50 (2H, s), 6.50 (1H, d, J=2.1), 6.60 (1H, d, J=7.4), 6.72 (1H, dd, J=7.4, 2.1), 7.28 (1H, d, J=7.4).
I-133	91-92°C	0.98 (3H, t, J=7.0), 1.23 (6H, s), 1.42-1.48 (2H, m), 1.70-1.80 (2H, m), 2.63 (3H, s), 2.65 (2H, s), 3.96 (2H, t, J=7.0), 4.50 (2H, s), 6.90 (2H, d, J=8.6), 6.98 (2H, d, J=8.6).
I-134	86-87°C	0.98 (3H, t, J=7.0), 1.23 (6H, s), 1.42-1.48 (2H, m), 1.70-1.80 (2H, m), 2.63 (3H, s), 2.65 (2H, s), 3.96 (2H, t, J=7.0), 4.50 (2H, s), 6.50 (1H, d, J=2.1), 6.60 (1H, d, J=7.8), 6.72 (1H, dd, J=7.8, 2.1), 7.28 (1H, d, J=7.8).

(Table 26)

Comp . No.	Physical Date	
No	M.p.	NMR($CHCl_3$)
I-135	69-70°C	1.22 (6H, s), 1.47 (3H, t, J=7.0), 2.64 (3H, s), 2.66 (2H, s), 3.88 (3H, s), 4.15 (2H, q, J=7.0), 4.51 (2H, s), 6.61 (1H, d, J=8.2), 6.62 (1H, d, J=2.1), 6.88 (1H, d, J=8.2).
I-136	88-89°C	1.04 (3H, t, J=7.0), 1.23 (6H, s), 1.80 (2H, sext, J=7.0), 2.63 (3H, s), 2.67 (2H, s), 3.87 (3H, s), 3.90 (2H, t, J=7.0), 4.51 (2H, s), 6.61 (1H, dd, J=8.2, 2.1), 6.62 (1H, d, J=2.1), 6.88 (1H, d, J=8.2).
I-137	83-85°C	0.98 (3H, t, J=7.0), 1.23 (6H, s), 1.42-1.48 (2H, m), 1.70-1.80 (2H, m), 2.64 (3H, s), 2.68 (2H, s), 3.87 (3H, s), 4.03 (2H, t, J=7.0), 4.50 (2H, s), 6.59 (1H, d, J=8.2), 6.61 (1H, s), 6.88 (1H, d, J=8.2).
I-138	84-85°C	1.23 (6H, s), 1.34 (6H, d, J=6.1), 2.63 (3H, s), 2.65 (2H, s), 4.50 (2H, s), 4.53 (1H, sept, J=6.1), 6.89 (2H, d, J=8.6), 7.04 (2H, d, J=8.6).
I-139	92-93°C	1.23 (6H, s), 1.34 (6H, d, J=6.1), 2.63 (3H, s), 2.65 (2H, s), 4.50 (2H, s), 4.53 (1H, sept, J=6.1), 6.50 (1H, d, J=2.1), 6.60 (1H, d, J=8.0), 6.72 (1H, dd, J=8.0, 2.1), 7.28 (1H, d, J=8.0).
I-140	109-110°C	1.22 (6H, s), 2.63 (3H, s), 2.65 (2H, s), 4.50 (2H, s), 7.04 (2H, d, J=7.5), 7.15 (1H, d, J=7.5), 7.32 (2H, t, J =7.5).
I-141	92-93°C	1.23 (6H, s), 2.63 (3H, s), 2.69 (2H, s), 4.54 (2H, s), 7.01-7.08 (1H, m), 7.11-7.15 (3H, m).
I-142	133-135°C	1.23 (6H, s), 2.63 (3H, s), 2.69 (2H, s), 4.54 (2H, s), 7.03 (1H, dd, J=8.0, 2.1), 7.08 (1H, dd, J=8.0, 2.1), 7.25 (1H, t, J=8.0), 7.44 (1H, t, J=8.0).
I-143	92-93°C	1.23 (6H, s), 2.63 (3H, s), 2.67 (2H, s), 4.50 (2H, s), 6.88 (1H, dd, J = 8.0, 2.1), 7.03 (1H, d, J=2.1), 7.15 (1H, dd, J=8.0, 2.1), 7.28(1H, t, J=8.0).
I-144	134-135°C	1.22 (6H, s), 2.22 (3H,s), 2.63 (3H, s), 2.65 (2H, s), 4.50 (2H, s), 7.00 (1H, d, J=8.1), 7.08 (1H, t, J=8.1), 7.15-7.25 (2H, m).
I-145	87-89°C	1.23 (6H, s), 2.37 (3H,s), 2.63 (3H, s), 2.66 (2H, s), 4.50 (2H, s), 6.82 (1H, d, J=8.1), 6.84 (1H, s), 6.98 (1H, d, J=8.1), 7.21 (1H, t, J=8.1).

(Table 27)

Comp . No.	Physical Date	
No	M.p.	NMR($CHCl_3$)
I-146	91-93°C	1.23 (6H, s), 2.35 (3H, s), 2.63 (3H, s), 2.65 (2H, s), 4.50 (2H, s), 6.92 (2H, d, J=8.6), 7.15 (2H, d, J=8.6).
I-147	82-83°C	0.90 (3H, t, J=7.0), 1.22 (6H, s), 1.28-1.40 (2H, m), 1.48-1.55 (2H, m), 2.55 (2H, t, J = 7.0), 2.64 (3H, s), 2.66 (2H, s), 4.50 (2H, s), 6.90 (1H, d, J=7.8), 7.09 (1H, t, J=7.8), 7.11 (1H, t, J=7.8), 7.28 (1H, d, J=7.8).
I-148	72-73°C	0.90 (3H, t, J=7.0), 1.22 (6H, s), 1.28-1.40 (2H, m), 1.48-1.55 (2H, m), 2.60 (2H, t, J=7.0), 2.64 (3H, s), 2.66 (2H, s), 4.50 (2H, s), 6.95 (2H, d, J=8.6), 7.18 (2H, d, J = 8.6).
I-149	133-134°C	1.23 (6H, s), 1.35 (9H, s), 2.65 (3H, s), 2.69 (2H, s), 4.50 (2H, s), 6.97 (1H, d, J=7.8), 7.13 (1H, t, J=7.8), 7.19 (1H, t, J=7.8), 7.41 (1H, d, J=7.8).
I-150	99-100°C	1.22 (6H, s), 1.23 (3H, t, J=7.4), 2.62 (3H, s), 2.64 (2H, s), 2.66 (2H, q, J=7.4), 4.50 (2H, s), 6.95 (2H, d, J= 8.6), 7.20 (2H, d, J=8.6).
I-151	40-42°C	1.23 (6H, s), 1.24 (3H, t, J=7.0), 2.64 (3H, s), 2.66 (2H, s), 2.67 (2H, q, J=7.0), 4.52 (2H, s), 6.83 (1H, d, J=8.1), 6.86 (1H, s), 7.00 (1H, d, J=8.1), 7.28 (1H, t, J=8.1).
I-152	118-119°C	1.23 (6H, s), 2.64 (3H, s), 2.67 (2H, s), 4.52 (2H, s), 6.97-7.10 (4H, m).
I-153	89-90°C	1.23 (6H, s), 2.64 (3H, s), 2.67 (2H, s), 4.52 (2H, s), 6.73-6.90 (3H, m), 7.25-7.30 (1H, m).
I-154	111-112°C	1.22 (6H, s), 1.25 (6H, d, J=7.0), 2.62 (3H, s), 2.64 (2H, s), 2.91 (1H, sept, J=7.0), 4.50 (2H, s), 6.95 (2H, d, J=8.6), 7.25 (2H, d, J=8.6).
I-155	127-129°C	1.23 (6H, s), 2.62 (3H, s), 2.64 (2H, s), 3.14-3.18 (4H, m), 3.85-3.90 (4H, m), 4.50 (2H, s), 6.93 (2H, d, J = 8.6), 7.04 (2H, d, J=8.6).
I-156	91-93°C	1.24 (6H, s), 2.62 (3H, s), 2.65 (3H, s), 2.68 (2H, s), 4.53 (2H, s), 7.21-7.25 (1H, m), 7.48 (1H, t, J=7.9), 7.61 (1H, t, J=1.8), 7.74-7.78 (1H, m).

(Table 28)

Comp . No.	Physical Date	
No	M.p.	NMR($CHCl_3$)
I-157	103.5-104.5°C	1.23 (6H, s), 2.63 (3H, s), 2.68 (2H, s), 4.50 (2H, s), 6.88-6.94 (2H, m), 7.46-7.51 (2H, m).
I-158	97-98°C	1.23 (6H, s), 2.64 (3H, s), 2.68 (2H, s), 4.51 (2H, s), 6.93-6.97 (1H, m), 7.19-7.31 (3H, m).
I-159	155.5-156.5°C	1.24 (6H, s), 2.65 (3H, s), 2.69 (2H, s), 4.54 (2H, s), 6.98-7.05 (2H, m), 7.28-7.34 (1H, m), 7.59-7.63 (1H, m).
I-160	102-106°C	1.23 (6H, s), 2.23 (3H, s), 2.64 (3H, s), 2.67 (2H, s), 4.00 (3H, s), 4.52 (2H, s), 7.01-7.05 (1H, m), 7.28 (1H, t, J=1.8), 7.37 (1H, t, J=7.8), 7.45-7.49 (1H, m).
I-161	111-112°C	1.23 (6H, s), 2.60 (3H, s), 2.65 (3H, s), 2.69 (2H, s), 4.53 (2H, s), 7.06-7.10 (2H, m), 7.97-8.03 (2H, m).
I-162	124-125°C	1.23 (6H, s), 2.23 (3H, s), 2.64 (3H, s), 2.67 (2H, s), 4.00 (3H, s), 4.52 (2H, s), 7.00-7.05 (2H, m), 7.65-7.70 (2H, m).
I-163	102-103.5°C	1.23 (6H, s), 1.32 (6H, d, J=6.3), 2.63 (2H, s), 2.64 (3H, s), 4.52 (2H, s), 4.52 (1H, sept, J=6.3), 6.90-6.98 (3H, m), 7.04-7.13 (1H, m)
I-164	90-92°C	0.94 (3H, t, J=7.3), 1.23 (6H, s), 1.58 (2H, sext, J=7.3), 2.51-2.56 (2H, m), 2.65 (3H, s), 2.65 (2H, s), 4.51 (2H, s), 6.90 (1H, dd, J=7.6, 1.3), 7.07-7.25 (3H, m)

(Table 28) (continued)

Comp . No.	Physical Date	
No	M.p.	NMR($CHCl_3$)
I-165	157-158°C	1.23 (6H, s), 2.64 (3H, s), 2.68 (2H, s), 4.49 (2H, s), 7.08 (1H, d, J=7.9), 7.22 (1H, d, J=7.6), 7.50-7.56 (1H, m), 7.66-7.69 (1H, m)
I-166	145-146°C	1.24 (6H, s), 2.64 (3H, s), 2.69 (2H, s), 4.51 (2H, s), 7.00-7.13 (7H, m), 7.30-7.37 (2H, m)
I-167	77-79°C	0.95 (3H, t, J=7.3), 1.23 (6H, s), 1.65 (2H, sext, J=7.3), 2.58 (2H, t, J=7.3), 2.63 (3H, s), 2.66 (2H, s), 4.51 (2H, s), 6.93-7.00 (2H, m), 7.14-7.20 (2H, m)

(Table 29)

Comp . No.	Physical Date	
No	M.p.	NMR($CHCl_3$)
I-168	117-118°C	1.23 (6H, s), 1.55 (9H, s), 2.63 (3H,s), 2.67 (2H, s), 4.52 (2H, s), 6.96-7.01 (2H, m), 7.37-7.42 (2H, m).
I-169	55-56°C	1.24 (6H, s), 2.65 (3H, s), 2.69 (2H, s), 4.53 (2H, s), 7.19 (1H, d, J=7.6), 7.26-7.27 (1H, m), 7.40-7.52 (2H, m).
I-170	88-90°C	1.24 (6H, s), 2.65 (3H, s), 2.69 (2H, s), 4.53 (2H, s), 7.10 (2H, d, J=8.2), 7.63 (2H, d, J=8.2).
I-171		1.15 (6H, s), 1.18 (6H, d, J=6.9), 2.17 (3H, s), 2.31 (3H, s), 2.64 (2H, s), 3.11 (1H, sept, J=6.9), 3.78 (2H, s), 6.80 (1H, d, J=8.2), 7.11-7.18 (1H, m), 7.28-7.35 (1H, m).
I-172		1.15 (6H, s), 1.18 (6H, d, J=6.9), 2.15 (3H, s), 2.31 (3H, s), 2.65 (2H, s), 3.11 (1H, sept, J=6.9), 3.78 (2H, s), 6.99 (1H, s), 7.11-7.18 (1H, m), 7.28-7.35 (1H, s).
I-173	121-123°C	1.22 (6H, s), 2.64 (3H, s), 2.67 (2H, s), 3.89 (3H, s), 3.89 (3H, s), 4.54 (2H, s), 6.96 (1H, d, J=8.6), 7.67 (1H, d, J=2.1), 7.87 (1H, dd, J=8.6, 2.1).
I-174	146-147°C	1.24 (6H, s), 2.59 (2H, s), 2.65 (3H, s), 2.96-2.99 (4H, m), 3.76-3.79 (4H, m), 4.52 (2H, s), 6.98-7.17 (4H, m).
I-175	155-157°C	1.23 (6H, s), 2.64 (3H, s), 2.66 (2H, s), 3.16-3.20 (4H, m), 3.84-3.88 (4H, m), 4.51 (2H, s), 6.54-6.57 (2H, m), 6.70-6.74 (1H, m), 7.24-7.30 (1H, m).
I-176		1.22 (6H, d, J=6.6), 1.23 (6H, s), 1.38 (3H, t, J=7.1), 2.65 (3H, s), 2.67 (2H, s), 3.08-3.18 (1H, m), 4.37 (2H, q, J=6.9), 4.52 (2H, s), 7.38 (1H, d, J=7.9), 7.59 (1H, d, J=2.0), 7.82 (1H, dd, J=8.1, 1.8).
I-177	120-122°C	1.23 (6H, s), 1.50-1.61 (2H, m), 1.67-1.75 (4H, m), 2.62 (3H, s), 2.66 (2H, s), 3.13-3.17 (4H, m), 4.50 (2H, s), 6.92-7.02 (4H, m).
I-178	124-125°C	1.23 (6H, s), 1.85-1.90 (4H, m), 2.62 (3H, s), 2.68 (2H, s), 3.22-3.27 (4H, m), 4.48 (2H, s), 6.74-6.80 (2H, m), 6.95-6.98 (1H, m), 7.03-7.10 (1H, m).

(Table 30)

Comp .No.	Physical Date	
No	M.p.	NMR($CHCl_3$)
I-179		1.23 (6H, s), 2.50 (3H, s), 2.64 (3H, s), 2.67 (2H, s), 4.51 (2H, s), 6.78-6.82 (1H, m), 6.91 (1H, t, J=2.0), 7.03-7.07 (1H, m), 7.25-7.31 (1H, m).
I-180	102-103°C	1.23 (6H, s), 2.49 (3H, s), 2.63 (3H, s), 2.67 (2H, s), 4.51 (2H, s), 6.96-7.01 (2H, m), 7.27-7.31 (2H, m).

(Table 30) (continued)

Comp .No.	Physical Date	
No	M.p.	NMR($CHCl_3$)
I-181	82-83°C	1.23 (6H, s), 2.64 (3H, s), 2.67 (2H, s), 4.52 (2H, s), 7.07 (1H, dd, J=7.6, 1.7), 7.14-7.20 (1H, m), 7.25-7.34 (2H, m).
I-182		1.23 (6H, s), 2.64 (3H, s), 2.69 (2H, s), 4.52 (2H, s), 6.90 (1H, s), 6.93-7.04 (2H, m), 7.38 (1H, t, J=8.2)
I-183	68-70°C	1.24 (6H, s), 2.64 (3H, s), 2.69 (2H, s), 4.51 (2H, s), 7.01-7.07 (2H, m), 7.21-7.24 (2H, m).
I-184	169-170°C	1.25 (6H, s), 2.66 (3H, s), 2.70 (2H, s), 4.54 (2H, s), 7.13-7.18 (2H, m), 7.34-7.39 (1H, m), 7.59-7.63 (2H, m), 7.86-7.91 (1H, m), 8.58 (1H, dd, J=4.8, 1.6), 8.87 (1H, t, J=1.5)
I-185	92.5-93.5°C	1.24 (6H, s), 2.65 (3H, s), 2.69 (2H, s), 4.54 (2H, s), 7.05-7.09 (1H, m), 7.24 (1H, t, J=1.6), 7.34-7.40 (2H, m), 7.49 (1H, t, J=7.6), 7.87-7.92 (1H, m), 8.60 (1H, dd, J=4.9, 1.4), 8.87 (1H, dd, J=2.3, 0.7)
I-186		1.09 (6H, s), 2.56 (3H, s), 2.58 (2H, s), 4.20 (2H, s), 7.09-7.12 (1H, m), 7.24-7.30 (2H, m), 7.36-7.45 (2H, m), 7.75-7.79 (1H, m), 8.54 (1H, dd, J=4.9, 1.6), 8.68 (1H, dd, J=2.3, 0.7)
I-187	110.5-111.5°C	1.17 (6H, s), 2.51 (3H, s), 2.61 (2H, s), 4.33 (2H, s), 6.93-7.19 (7H, m), 7.23-7.30 (2H, m)
I-188	75-76°C	1.14 (6H, s), 1.43 (6H, t, J=7.4), 2.61 (2H, s), 3.65 (2H, s), 3.84 (3H, s), 4.08 (4H, q, J=7.4), 6.46 (1H, dd, J=8.1, 2.2), 6.52 (1H, d, J=2.2), 6.84 (1H, d, J=8.4).
I-189		1.19 (6H, s), 2.61 (2H, s), 3.65 (2H, s), 3.85 (3H, s), 3.88 (3H, s), 6.85-6.99 (3H, m), 7.02-7.15 (1H, m).

(Table 31)

Comp . No.	Physical Date	
No	M.p.	NMR($CHCl_3$)
I-190		1.13 (6H, s), 1.23 (3H, t, J=7.4), 2.62 (2H, s), 2.66 (2H, q, J=7.4), 3.64 (2H, s), 3.84 (3H, s), 6.84 (2H, d, J=8.6), 7.16 (2H, d, J=8.6).
I-191	45-47°C	1.14 (6H, s), 1.25 (6H, d, J= 7.0), 2.62 (2H, s), 2.91 (1H, sept, J=7.0), 3.64 (2H, s), 3.84 (3H, s), 6.86 (2H, d, J=8.6), 7.19 (2H, d, J=8.6).
I-192	93-95°C	1.15 (6H, s), 2.31 (3H, s), 2.62 (2H, s), 3.80 (2H, s), 3.85 (3H, s), 6.85-6.99 (3H, m), 7.02-7.15 (1H, m).
I-193	65-67°C	1.13 (6H, s), 1.23 (3H, t, J=7.4), 2.31 (3H, s), 2.62 (2H, s), 2.65 (2H, q, J=7.4), 3.77 (2H, s), 6.90 (2H, d, J=8.3), 7.21 (2H, d, J=8.3).
I-194	95-97°C	1.15 (6H, s), 1.24 (6H, d, J=7.0), 2.31 (3H, s), 2.64 (2H, s), 2.91 (1H, sept, J=7.0), 3.77 (2H, s), 6.90 (2H, d, J=8.6), 7.21 (2H, d, J=8.6).
I-195	94-96°C	1.15 (6H, s), 1.41 (3H, t, J=7.0), 2.31 (3H, s), 2.64 (2H, s), 3.77 (2H, s), 4.05 (2H, q, J=7.4), 6.90-6.99 (4H, m).
I-196	99-100°C	1.15 (6H, s), 1.47 (3H, t, J=7.0), 2.32 (3H, s), 2.66 (2H, s), 3.77 (2H, s), 3.88 (3H, s), 4.08 (2H, q, J=7.0), 6.52 (1H, d, J= 8.2), 6.56 (1H, d, J=2.1), 6.88 (1H, d, J=8.2).
I-197	133-134°C	1.23 (6H, s), 1.50-1.75 (6H, m), 2.63 (3H, s), 2.65 (2H, s), 3.18 (4H, t, J=5.4), 4.51 (2H, s), 6.47-6.57 (2H, m), 6.72-6.76 (1H, m), 7.21 (1H, d, J=8.1)
I-198	124-125°C	1.17 (6H, t, J=6.9), 1.23 (6H, s), 2.61 (3H, s), 2.68 (2H, s), 3.35 (4H, q, J=6.9), 4.49 (2H, s), 6.68 (2H, d, J=8.9), 7.04 (2H, d, J=8.9)

(Table 31) (continued)

Comp . No.	Physical Date	
No	M.p.	NMR($CHCl_3$)
I-199	85-87°C	1.22 (6H, s), 2.63 (3H, s), 2.67 (2H, s), 3.89 (3H, s), 3.92 (3H, s), 4.54 (2H, s), 7.01 (1H, d, J=7.9), 7.62 (1H, d, J=1.3), 7.67 (1H, dd, J=7.9, 1.7)
I-200	137-138°C	1.23 (6H, s), 2.11-2.22 (2H, m), 2.62 (2H, t, J=7.9), 2.64 (3H, s), 2.67 (2H, s), 3.88 (2H, t, J=7.1), 4.52 (2H, s), 6.81-6.84 (1H, m), 7.30-7.50 (3H, m)

(Table 32)

Comp . No.	Physical Date	
No	M.p.	NMR($CHCl_3$)
I-201	86.5-87.5°C	1.22 (6H, s), 2.62 (3H, s), 2.67 (2H, s), 4.50 (2H, s), 6.71 (1H, t, J=2.0), 6.76-6.82 (2H, m), 7.02-7.13 (3H, m), 7.29-7.37 (3H, m)
I-202	162-163°C	1.25 (6H, s), 2.65 (3H, s), 2.70 (2H, s), 4.54 (2H, s), 7.10-7.14 (2H, m), 7.33-7.46 (3H, m), 7.59-7.63 (4H, m)
I-203	56.5-57.5°C	1.06 (6H, s), 2.51 (3H, s), 2.59 (2H, s), 4.14 (2H, s), 7.07 (1H, dd, J=8.2, 1.3), 7.21-7.45 (8H, m)
I-204	97-99°C	1.24 (6H, s), 2.65 (3H, s), 2.68 (2H, s), 4.54 (2H, s), 7.00-7.04 (1H, m), 7.25-7.26 (1H, m), 7.33-7.48 (5H, m), 7.60-7.63 (2H, m)
I-205	95-96°C	1.21 (6H, s), 1.21 (6H, d, J=6.9), 2.61 (2H, s), 4.13(3H, s), 4.16 (2H, s), 6.77-6.81 (1H, m), 7.13-7.16 (2H, m), 7.29-7.33 (1H, m)
I-206	128-129°C	1.18 (6H, d, J=6.9), 1.22 (6H, s), 2.63 (3H, s), 2.66 (2H, s), 2.96-3.06 (1H, m), 4.48 (2H, s), 6.67 (1H, d, J=8.2), 7.47 (1H, dd, J=8.2, 1.7), 7.59 (1H, d, J=2.0)
I-207	149-150°C	1.23 (6H, s), 2.63 (3H, s), 2.67 (2H, s), 3.71 (8H, m), 3.86 (3H, s), 4.53 (2H, s), 6.95-7.05 (3H, m)
I-208	124-126°C	1.23 (6H, s), 2.61 (3H, s), 2.67 (2H, s), 2.96 (6H, s), 4.50 (2H, s), 6.74 (2H, d, J=8.2), 7.04 (2H, d, J=8.2).
I-209	107-109°C	1.23 (6H, s), 2.63 (3H, s), 2.65 (2H, s), 2.96 (6H, s), 4.51 (2H, s), 6.34 (1H, d, J=2.0), 6.38 (1H, d, J=8.0), 6.54 (1H, dd, J=8.0, 2.0), 7.24 (2H, d, J=8.0).
I-210	98-99°C	1.06 (3H, t, J=7.4), 1.23 (6H, s), 2.63 (5H, s), 2.65 (3H, s), 2.99 (2H, q, J=7.4), 4.51 (2H, s), 6.98-7.10 (3H, m), 7.15-7.20 (1H, m).
I-211	94-96°C	0.84 (3H, t, J = 7.4), 1.22 (6H, s), 1.49 (2H, sext, J = 7.3), 2.63 (3H, s), 2.65 (2H, s), 2.72 (3H, s), 2.84 (2H, t, J = 7.4), 4.51 (2H, s), 6.90-7.05 (3H, m), 7.10-7.15 (1H, m).

(Table 33)

Comp . No.	Physical Date	
No	M.p.	NMR($CHCl_3$)
I-212	98-99°C	1.02 (6H, t, J=7.4), 1.22 (6H, s), 2.61 (2H, s), 2.63 (3H, s), 3.06 (4H, q, J=7.4), 4.51 (2H, s), 6.98-7.10 (4H, m).
I-213	83-84°C	1.23 (6H, s), 2.64 (3H, s), 2.71 (2H, s), 4.57 (2H, s), 6.90-7.12 (3H, m)
I-214		1.19 (6H, d, J=6.9), 1.23 (6H, s), 2.64 (3H, s), 2.67 (2H, s), 3.06 (1H, sept, J=6.9), 4.49 (2H, s), 6.85 (1H, d, J=8.2), 7.14 (1H, dd, J=8.2, 2.3), 7.27 (1H, d, J=2.3)
I-215	83-85°C	1.23 (6H, s), 2.32 (3H, s), 2.63 (3H, s), 2.66 (2H, s), 2.71 (6H, s), 4.50 (2H, s), 6.75-6.80 (1H, m), 6.98 (1H, s), 6.97-7.00 (1H, m).

(Table 33) (continued)

Comp . No.	Physical Date	
No	M.p.	NMR($CHCl_3$)
I-216	99-100°C	1.23 (6H, s), 2.33 (3H, s), 2.62 (3H, s), 2.65 (2H, s), 2.70 (6H, s), 4.50 (2H, s), 6.78 (2H, t, J=7.9), 6.91 (1H, d, J=7.9).
I-217	98-99°C	1.23 (6H, s), 2.30 (3H, s), 2.63 (3H, s), 2.64 (2H, s), 2.67 (6H, s), 4.50 (2H, s), 6.81 (1H, s), 6.92 (2H, s).
I-218	117-19°C	1.23 (6H, s), 2.63 (3H, s), 2.65 (2H, s), 2.68 (6H, s), 4.50 (2H, s), 6.89 (1H, d, J=8.5), 6.99 (1H, d, J=2.0), 7.04 (1H, dd, J=7.9, 2.0).
I-219	68-70°C	1.22 (6H, s), 2.22 (6H, s), 2.64 (3H, s), 2.66 (2H, s), 4.54 (2H, s), 6.93-6.98 (1H, m), 7.04 (2H, d, J=8.0).
I-220	97-99°C	1.22 (6H, s), 1.34 (3H, t, J=7.4), 2.64 (2H, s), 2.72 (6H, s), 3.25 (2H, q, J=7.4), 4.47 (2H, s), 6.94-7.05 (3H, m), 7.15-7.20 (1H, m).
I-221	118-119°C	1.22 (6H, s), 1.34 (3H, t, J=7.4), 2.64 (2H, s), 2.95 (6H, s), 3.25 (2H, q, J=7.4), 4.47 (2H, s), 6.34 (1H, d, J=7.5), 6.38 (1H, s), 6.52 (1H, d, J=7.5), 7.24 (1H, t, J=7.5).
I-222	74-76°C	1.22 (6H, s), 1.34 (3H, t, J=7.4), 2.33 (3H, s), 2.63 (2H, s), 2.70 (6H, s), 3.25 (2H, q, J=7.4), 4.47 (2H, s), 6.78 (1H, d, J=7.5), 6.82 (1H, s), 6.91 (1H, t, J=7.5).

(Table 34)

Comp . No.	Physical Date	
No	M.p.	NMR($CHCl_3$)
I-223		1.22 (6H, s), 1.25 (6H, d, J=7.0), 1.34 (3H, t, J=7.4), 2.65 (2H, s), 2.91 (1H, sept, J=7.0), 3.25 (2H, q, J=7.4), 4.50 (2H, s), 6.98 (2H, d, J=8.2), 7.28 (2H, d, J = 8.2).
I-224		1.21 (6H, s), 2.62 (3H, s), 2.66 (2H, s), 2.97 (3H, d, J=4.9), 3.84 (3H, s), 4.51 (2H, s), 6.66 (1H, brs), 6.96 (1H, d, J=7.9), 7.30-7.33 (1H, m), 7.49 (1H, d, J=1.3)
I-225	69-71°C	1.23 (6H, s), 2.64 (3H, s), 2.68 (2H, s), 4.52 (2H, s), 6.49 (1H, t, J=74.6), 7.04-7.26 (4H, m)
I-226		1.23 (6H, s), 2.64 (3H, s), 2.68 (2H, s), 4.51 (2H, s), 6.50 (1H, t, J=74.2), 7.00-7.05 (2H, s), 7.11-7.16 (2H, m)
I-227	81-83°C	1.17 (6H, t, J=7.0), 1.23 (6H, s), 2.63 (3H, s), 2.66 (2H, s), 3.35 (4H, q, J=7.0), 4.52 (2H, s), 6.29 (1H, s), 6.30 (1H, dt, J=8.2,2.3), 6.49 (1H, dd, J=8.2, 2.3), 7.19 (1H, t, J=8.2).
I-228	106-107°C	1.21 (6H, s), 2.61 (3H, s), 2.64 (2H, s), 2.70 (6H, s), 4.47 (2H, s), 6.90 (2H, s), 6.93 (1H, s).
I-229	121-122°C	1.23 (6H, s), 2.62 (3H, s), 2.65 (2H, s), 2.70 (6H, s), 4.48 (2H, s), 6.50-6.70 (2H, m), 6.93 (1H, dd, J=8.5, 6.2).
I-230	85-86°C	1.21 (6H, s), 2.63 (3H, s), 2.64 (2H, s), 2.66 (6H, s), 4.49 (2H, s), 6.74-6.79 (2H, m), 6.93-6.98 (1H, m).
I-231	82-84°C	1.23 (6H, s), 1.25 (3H, t, J=7.6), 2.62 (3H, s), 2.66 (2H, s), 2.67 (2H, q, J=7.6), 2.71 (6H, s), 4.50 (2H, s), 6.80 (1H, d, J=7.6), 6.84 (1H, s), 6.93 (1H, d, J=7.6).
I-232	75-76°C	1.22 (3H, t, J=7.6), 1.23 (6H, s), 2.60 (2H, q, J=7.6), 2.63 (3H, s), 2.64 (2H, s), 2.68 (6H, s), 4.50 (2H, s), 6.83 (1H, s), 6.93 (2H, s).
I-233	86-88°C	1.22 (6H, s), 1.33 (3H, t, J=7.4), 2.64 (2H, s), 2.71 (6H, s), 3.24 (2H, q, J=7.4), 4.47 (2H, s), 6.92 (2H, s), 6.94(1H, s).

(Table 35)

Comp . No.	Physical Date	
No	M.p.	NMR($CHCl_3$)
I-234	70-71°C	1.22 (6H, s), 1.34 (3H, t, J=7.4), 2.64 (2H, s), 2.71 (6H, s), 3.25 (2H, q, J=7.4), 4.46 (2H, s), 6.60-6.68 (2H, m), 6.92-6.94(1H, m).
I-235	80-82°C	1.22 (6H, s), 1.24 (3H, t, J=7.6), 1.33 (3H, t, J=7.4), 2.60 (2H, q, J=7.6), 2.61 (2H, s), 2.71 (6H, s), 3.24 (2H, q, J=7.4), 4.47 (2H, s), 6.81 (1H, d, J=7.6), 6.94(1H, s), 6.94 (1H, d, J=7.6).
I-236		1.03 (3H, t, J=7.3), 1.20 (6H, d, J=6.9), 1.23 (6H, s), 1.40 (3H, d, J=6.9), 1.61-1.89 (2H, m), 2.63 (2H, s), 3.15 (1H, sept, J=6.9), 3.95 (1H, q, J=6.9), 4.47 (2H, s), 6.89-6.92 (1H, m), 7.13-7.20 (2H, m), 7.31-7.34 (1H, m)
I-237		1.05 (6H, d, J=6.6), 1.21 (6H, d, J=6.6), 1.23 (6H, s), 1.98-2.08 (1H, m), 2.64 (2H, s), 3.16 (1H, sept, J=6.6), 3.20 (2H, d, J=6.6), 4.49 (2H, s), 6.88-6.92 (1H, m), 7.13-7.22 (2H, m), 7.30-7.35 (1H, m)
I-238	102-104°C	1.20 (6H, d, J=6.9), 1.22 (6H, s), 2.61 (2H, s), 2.85-2.95 (1H, m), 3.19 (3H, d, J=4.6), 4.46 (2H, s), 6.73-6.79 (1H, m), 7.14-7.20 (2H, m), 7.29-7.34 (1H, m), 12.40 (1H, brs)
I-239	58-60°C	1.23 (6H, s), 2.17 (3H, s), 2.64 (3H, s), 2.65 (2H, s), 2.70 (6H, s), 4.52 (2H, s), 6.63 (1H, d, J=7.9), 6.87 (1H, d, J=7.9), 7.14 (1H, d, J=7.9).
I-240	100-101°C	1.23 (6H, s), 2.62 (3H, s), 2.64 (2H, s), 2.78 (6H, s), 3.89 (3H, s), 4.52 (2H, s), 6.60-6.70 (2H, m), 6.94 (1H, d, J=7.9).
I-241	82-83°C	1.23 (6H, s), 2.30 (3H, s), 2.63 (3H, s), 2.65 (2H, s), 2.70 (6H, s), 4.52 (2H, s), 6.63 (1H, dt, J=7.9,1.9), 6.70 (1H, d, J=1.9), 7.14 (1H, d, J=7.9).
I-242	99-100°C	1.23 (6H, s), 2.63 (3H, s), 2.68 (2H, s), 2.81 (6H, s), 4.50 (2H, s), 6.91 (1H, dt, J=8.4, 2.6), 7.06 (1H, d, J=8.4), 7.14 (1H, d, J=2.6).
I-243	63-64°C	1.23 (6H, s), 2.63 (3H, s), 2.67 (2H, s), 2.78 (6H, s), 3.89 (3H, s), 4.52 (2H, s), 6.67 (1H, s), 6.70 (1H, d, J=7.9), 6.81 (1H, d, J=7.9).
I-244	68-70°C	0.88 (6H, t, J=7.5), 1.22 (6H, d, J=6.9), 1.35 (3H, t, J=7.4), 1.50-1.70 (4H, m), 2.61 (2H, s), 3.15 (1H, sept, J=6.9), 3.29 (2H, q, J=7.4), 4.44 (2H, s), 6.89-6.92 (1H, m), 7.08-7.21 (2H, m), 7.30-7.35 (1H, m).

(Table 36)

Comp No.	Physical Date	
No	M.p.	NMR($CHCl_3$)
I-245	81-82°C	1.14 (6H, s), 1.20 (6H, d, J=6.9), 2.63 (2H, s), 3.06 (2H, s), 3.08 (1H, sept, J=6.9), 3.18 (3H, s), 6.74 (1H, dd, J=7.3, 1.7), 6.98-7.10 (2H, m), 7.20-7.24 (1H, m)
I-246	47-49°C	0.95 (3H, t, J=7.3), 1.13 (6H, s), 1.20 (6H, d, J=6.9), 1.55-1.74 (2H, m), 2.62 (2H, s), 3.03-3.11 (3H, m), 3.52-3.57 (2H, m), 6.73 (1H, dd, J=7.6, 1.7), 6.96-7.10 (2H, m), 7.21 (1H, dd, J=7.3, 1.7)
I-247	68-70°C	1.11 (6H, s), 1.18 (6H, d, J=6.9), 1.19 (6H, d, J=6.9), 2.56 (2H, s), 2.89 (2H, s), 3.08 (1H, sept, J=6.9), 5.08 (1H, sept, J=6.9), 6.73 (1H, dd, J=7.9, 1.7), 6.99-7.10 (2H, m), 7.21 (1H, dd, J=7.9, 1.7)
I-248		0.97 (6H, d, J=6.9), 1.14 (6H, s), 1.18 (6H, d, J=6.9), 2.05-2.15 (1H, in), 2.62 (2H, s), 3.07 (2H, s), 3.08 (1H, sept, J=6.9), 3.44 (2H, d, J=7.6), 6.71(1H, dd, J=7.6, 1.7), 6.96-7.09 (2H, m), 7.21 (1H, dd, J=7.6, 1.7)
I-249	96-97°C	1.23 (6H, s), 2.64 (3H, s), 2.68 (2H, s), 4.59 (2H, s), 7.04 (1H, d, J=7.3), 7.41-7.50 (3H, m), 7.67 (1H, d, J=7.3), 7.87 (1H, dd, J = 7.3, 2.1), 8.05 (1H, d, J=7.3).

(Table 36) (continued)

Comp No.	Physical Date	
No	M.p.	NMR($CHCl_3$)
I-250	108-109°C	1.24 (6H, s), 2.67 (3H, s), 2.69 (2H, s), 4.59 (2H, s), 7.15 (1H, d, J=7.3), 7.41 (1H, q, J=7.3), 7.69 (1H, t, J=8.4), 7.91 (1H, d, J=7.3), 8.45 (1H, d, J=8.4), 8.92-8.95 (1H, m).
I-251	105-107°C	1.22 (6H, s), 2.62 (3H, s), 2.65 (2H, s), 3.97 (3H, s), 4.53 (2H, s), 6.87-6.90 (1H, m), 7.25-7.30 (1H, m), 7.96-7.99 (1H, m).
I-252	132-133°C	1.23 (6H, s), 2.63 (3H, s), 2.68 (2H, s), 2.92 (3H, s), 4.49 (2H, s), 6.73-6.78 (1H, m), 7.20-7.23 (1H, m), 8.05-8.07 (1H, m)
I-253	118-120°C	1.23 (6H, s), 2.60 (3H, s), 2.63 (2H, s), 4.52 (2H, s), 7.30 (2H, s), 8.12 (1H, s).
I-254	112-113°C	1.23 (6H, s), 2.63 (3H, s), 2.69 (2H, s), 3.94 (3H, s), 4.51 (2H, s), 6.76 (1H, d, J = 8.1), 7.35 (1H, dd, J = 8.1, 2.1), 7.92 (1H, d, J = 2.1).
I-255	109-110°C	1.23 (6H, s), 1.40 (3H, t, J=7.0), 2.62 (3H, s), 2.66 (2H, s), 4.38 (2H, q, J=7.0), 4.51 (2H, s), 6.75 (1H, d, J= 8.1). 7.35 (1H, dd, J=8.1, 2.1), 7.90 (1H, d, J=2.1).

(Table 37)

	Physical Date	
No	M.p.	NMR($CHCl_3$)
I-256	75-76°C	1.03 (3H, t, J=7.6), 1.22 (6H, s), 1.76 (2H, sext, J= 7.6), 2.63 (3H, s), 2.65 (2H, s), 4.24 (2H, t, J=7.6), 4.51 (2H, s), 6.76 (1H, d, J=8.1), 7.35 (1H, dd, J=8.1, 2.1), 7.92 (1H, d, J=2.1).
I-257	74-76°C	1.24 (6H, s), 1.36 (6H, d, J=6.3), 2.63 (3H, s), 2.70 (2H, s), 4.51 (2H, s), 5.28 (1H, sept, J=6.3), 6.70 (1H, d, J=8.1), 7.32 (1H, dd, J=8.1, 2.1), 7.92 (1H, d, J=2.1).
I-258	102-104°C	1.23 (6H, s), 2.58 (3H, s), 2.63 (2H, s), 2.69 (3H, s), 4.51 (2H, s), 7.20-7.26 (2H, m), 8.21 (1H, d, J=2.1).
I-259	81-83°C	1.23 (6H, s), 1.38 (3H, t, J=7.3), 2.63 (3H, s), 2.63 (2H, s), 3.18 (2H, q, J=7.3), 4.51 (2H, s), 7.15-7.26 (2H, m), 8.21 (1H, d, J=2.1).
I-260	78-79°C	1.05 (3H, t, J = 7.4), 1.23 (6H, s), 1.75 (2H, sext, J=7.3), 2.63 (3H, s), 2.65 (2H, s), 3.15 (2H, t, J=7.4), 4.51 (2H, s), 7.15-7.26 (2H, m), 8.20 (1H, d, J=2.1).
I-261	102-103°C	1.23 (6H, s), 1.40 (6H, d, J=6.6), 2.63 (3H, s), 2.66 (2H, s), 4.00 (1H, sept, J=6.6), 4.51 (2H, s), 7.15-7.26 (2H, m), 8.22 (1H, d, J=2.1).
I-262	109-110°C	1.22 (6H, s), 2.61 (3H, s), 2.65 (2H, s), 2.70 (6H, s), 3.80 (3H, s), 4.48 (2H, s), 6.47 (1H, dd, J=7.9, 2.1), 6.56 (1H, d, J=2.1), 6.95 (1H, d, J=7.9).
I-263	99-100°C	1.22 (6H, s), 2.62 (3H, s), 2.63 (2H, s), 2.64 (6H, s), 3.78 (3H, s), 4.48 (2H, s), 6.59 (1H, d, J=2.1), 6.64 (1H, dd, J=7.9, 2.1), 6.98 (1H, d, J=7.9).
I-264	114-115°C	0.98 (6H, t, J=7.0), 1.23 (6H, s), 2.16 (3H, s), 2.63 (3H, s), 2.64 (2H, s), 2.98 (4H, q, J=7.0), 4.52 (2H, s), 6.65 (1H, d, J=7.9), 6.89 (1H, d, J=7.9), 7.13 (1H, t, J=7.9).
I-265	66-67°C	0.98 (6H, t, J=7.0), 1.23 (6H, s), 2.16 (3H, s), 2.63 (3H, s), 2.64 (2H, s), 2.98 (4H, q, J=7.0), 4.52 (2H, s), 6.63 (1H, dd, J=7.9,2.1), 6.70 (1H, d, J=2.1), 7.16 (1H, d, J = 7.9).
I-266	88-90°C	1.04 (6H, t, J=7.0), 1.24 (6H, s), 2.63 (3H, s), 2.67 (2H, s), 3.17 (4H, q, J=7.0), 3.86 (3H, s), 4.51 (2H, s), 6.67 (1H, s), 6.70 (1H, d, J=7.9), 6.85 (1H, d, J=7.9).

(Table 38)

Comp . No.	Physical Date	
No	M.p.	NMR($CHCl_3$)
I-267	138-140°C	0.82-0.92 (9H, m), 1.18 (3H, d, J=6.9), 1.51-1.65 (6H, m), 2.62 (2H, s), 2.65 (3H, s), 2.87 (1H, sept, J=6.9), 4.33 (1H, d, J=13.5), 4.59 (1H, d, J=13.5), 6.89-6.92 (1H, m), 7.13-7.28 (3H, m)
I-268	161-163°C	0.89-0.95 (6H, m), 1.21 (6H, d, J=6.9), 1.25-1.54 (8H, m), 2.62 (2H, s), 2.65 (3H, s), 3.10 (1H, sept, J=6.9), 4.47 (2H, s), 6.88-6.92 (1H, m), 7.14-7.18 (2H, m), 7.31-7.34 (1H, m)
I-269		1.21 (6H, d, J=6.9), 1.65-1.88 (8H, m), 2.64 (3H, s), 2.75 (2H, s), 3.09 (1H, sept, J=6.9), 4.57 (2H, s), 6.90-6.94 (1H, m), 7.13-7.20 (2H, m), 7.30-7.35 (1H, m)
I-270		1.21 (6H, d, J=6.9), 1.37-1.54 (8H, m), 1.76-1.80 (2H, m), 2.65 (3H, s), 2.67 (2H, s), 3.09 (1H, sept, J=6.9), 4.54 (2H, s), 6.89 (1H, m), 7.11-7.21 (2H, m), 7.29-7.34 (1H, m)

(Table 39)

Comp No.		Physical Date
No	M.p.	NMR($CHCl_3$)
I-271		1.04 (3H, s), 1.08 (3H, s), 1.29 (6H, d), J=6.9), 2.69(2H, s), 3.40 (1H, sept, J=6.9), 3.43 (3H, s), 3.51 (2H, s), 7.18-7.29 (2H, m), 7.36-7.45 (2H, m)
I-272		0.96 (3H, s), 1.05 (3H, s), 1.25 (3H, d, J=6.9), 1.26 (3H, d, J=6.9), 2.61 (1H, d, J=12), 2.70 (1H, d, J=12), 3.39 (1H, sept, J=6.9), 3.45-3.58 (2H, m), 7.02-7.07 (2H, m), 7.11-7.18 (1H, m), 7.38-7.45 (2H, m), 7.61-7.70 (2H, m)
I-273		0.84 (3H, s), 1.00 (3H, s), 1.25 (3H, d, J=6.9), 1.29 (3H, J=6.9), 2.43 (3H, s), 2.53 (1H, d, J=12), 2.64 (1H, d, J=12), 3.29 (1H, d, J=16), 3.42 (1H, d, J=16), 3.47 (1H, sept, J=6.9), 7.09-7.19 (2H, m), 7.24-7.29 (2H, m), 7.38-7.45 (2H, m), 7.81-7.86 (2H, m)
I-274		0.99 (6H, s), 1.19 (6H, d, J=6.9), 2.40 (3H, s), 2.67 (2H, s), 2.87 (1H, sept, J=6.9), 3.43 (2H, s), 7.11-7.29 (6H, m), 7.68 (2H, d, J=8.1)
I-275		1.07 (6H, s), 1.26 (6H, d, J=6.9), 1.38 (3H, t, J=7.2), 2.71 (2H, s), 2.93 (1H, sept, J=6.9), 3.51 (2H, s), 3.60 (2H, q, J=7.2), 7.20-7.30 (4H, m)
I-276		1.19 (6H, s), 1.23 (6H, d, J=6.9), 2.77 (2H, s), 2.87 (1H, sept, J=6.9), 3.58 (2H, s), 6.65-6.69 (2H, m), 6.91 (1H, d, J=7.5), 7.20 (1H, t, J=7.5), 7.51 (2H, d, J=9.3), 8.22 (2H, d, J=9.3)
I-277		0.99 (6H, s), 1.20 (6H, d, J=6.9), 2.67 (2H, s), 2.88 (1H, sept, J=6.9), 3.44 (2H, s), 3.85 (3H, s), 6.86-6.90 (2H, m), 7.11-7.26 (4H, m), 7.72-7.76 (2H, m)

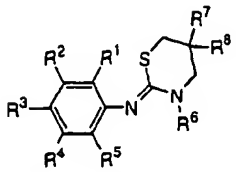
(Table 40)

Comp No.	Physical Date	
No	M.p.	NMR($CHCl_3$)
I-278		1.03 (6H, s), 1.20 (6H, d, J=6.9), 2.70 (2H, s), 2.88 (1H, sept, J=6.9), 3.44 (2H, s), 7.08-7.31 (4H, m), 7.60 (1H, t, J=8.4), 8.04 (1H, d, J=8.4), 8.39 (d, J=8.4), 8.74 (1H, s)
I-279		1.01 (6H, s), 1.19 (6H, d, J=6.9), 2.69 (2H, s), 2.88 (1H, sept, J=6.9), 3.42 (2H, s), 7.09-7.32 (4H, m), 7.68 (2H, d, J=8.4), 7.92 (2H, d, J=8.4),
I-280		1.19 (3H, s), 1.21 (3H, s), 1.23-1.30 (6H, m), 2.62 (1H, d, J=12), 2.82 (1H, sept, J=6.9), 3.02 (1H, d, J=12), 3.46-3.70 (2H, m), 6.53-6.60 (2H, m), 6.86 (1H, d, J=7.8), 7.13 (1H, t, J=7.8), 7.28-7.40 (2H, m), 7.61-7.66 (1H, m), 7.90 (1H, dd, J=7.5, 1.2)

[0142] The following compounds are within the scope of the present invention. These compounds can be prepared

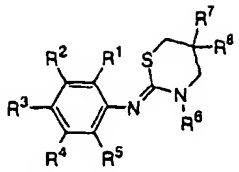
in accordance with the above examples. The numbers of left column in Table represent Compound No.

(Table 41-A)



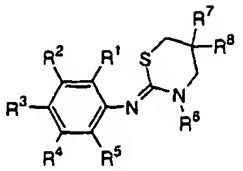
	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
A-1	H	Pr	H	H	H	CSSMe	Me	Me
A-2	Pr^i	H	Cl	H	H	CSSMe	Me	Me
A-3	H	Bu^s	H	H	H	CSSMe	Me	Me
A-4	H	H	Bu^s	H	H	CSSMe	Me	Me
A-5	OPr	H	H	H	H	CSSMe	Me	Me
A-6	OBu	H	H	H	H	CSSMe	Me	Me
A-7	H	SEt	H	H	H	CSSMe	Me	Me
A-8	H	H	SEt	H	H	CSSMe	Me	Me
A-9	H	SPr^i	H	H	H	CSSMe	Me	Me
A-10	H	H	SPr^i	H	H	CSSMe	Me	Me
A-11	H	$OCHF_2$	H	H	H	CSSMe	Me	Me
A-12	Pr^i	H	NMe_2	H	H	CSSMe	Me	Me
A-13	Pr^i	NMe_2	H	H	H	CSSMe	Me	Me
A-14	Et	Et	H	H	H	CSSMe	Me	Me
A-15	H	Et	Et	H	H	CSSMe	Me	Me
A-16	Bu^i	H	H	H	H	CSSMe	Me	Me
A-17	H	Bu^i	H	H	H	CSSMe	Me	Me
A-18	H	H	Bu^i	H	H	CSSMe	Me	Me
A-19	H	N(Me)Et	H	H	H	CSSMe	Me	Me
A-20	H	N(Me)Pr	H	H	H	CSSMe	Me	Me
A-21	NPr_2	H	H	H	H	CSSMe	Me	Me
A-22	H	NPr_2	H	H	H	CSSMe	Me	Me
A-23	H	H	NPr_2	H	H	CSSMe	Me	Me
A-24	H	NPr_2	Me	H	H	CSSMe	Me	Me
A-25	H	Bu^i	H	H	H	CSSMe	Me	Me

(Table 41-B)



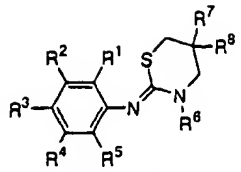
	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
A-26	H	CH_2OMe	H	H	H	CSSMe	Me	Me
A-27	H	H	CH_2OMe	H	H	CSSMe	Me	Me
A-28	CH_2OEt	H	H	H	H	CSSMe	Me	Me
A-29	H	CH_2OEt	H	H	H	CSSMe	Me	Me
A-30	H	H	CH_2OEt	H	H	CSSMe	Me	Me
A-31	CH_2SMe	H	H	H	H	CSSMe	Me	Me
A-32	H	CH_2SMe	H	H	H	CSSMe	Me	Me
A-33	H	H	CH_2SMe	H	H	CSSMe	Me	Me
A-34	CH_2SEt	H	H	H	H	CSSMe	Me	Me
A-35	H	CH_2SEt	H	H	H	CSSMe	Me	Me
A-36	H	H	CH_2SEt	H	H	CSSMe	Me	Me
A-37	CH_2NMe_2	H	H	H	H	CSSMe	Me	Me
A-38	H	CH_2NMe_2	H	H	H	CSSMe	Me	Me
A-39	H	H	CH_2NMe_2	H	H	CSSMe	Me	Me
A-40	CH_2NEt_2	H	H	H	H	CSSMe	Me	Me
A-41	H	CH_2NEt_2	H	H	H	CSSMe	Me	Me
A-42	H	H	CH_2NEt_2	H	H	CSSMe	Me	Me
A-43	OCH_2CH_2Ome	H	H	H	H	CSSMe	Me	Me
A-44	H	OCH_2CH_2OMe	H	H	H	CSSMe	Me	Me
A-45	H	H	OCH_2CH_2OMe	H	H	CSSMe	Me	Me
A-46	OCH_2CH_2SMe	H	H	H	H	CSSMe	Me	Me
A-47	H	OCH_2CH_2SMe	H	H	H	CSSMe	Me	Me
A-48	H	H	OCH_2CH_2SMe	H	H	CSSMe	Me	Me
A-49	$OCH_2CH_2NMe_2$	H	H	H	H	CSSMe	Me	Me
A-50	H	$OCH_2CH_2NMe_2$	H	H	H	CSSMe	Me	Me

(Table 41-C)



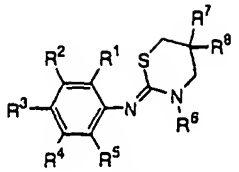
	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
A-51	H	H	$OCH_2CH_2NMe_2$	H	H	CSSMe	Me	Me
A-52	F	H	F	H	H	CSSMe	Me	Me
A53	Cl	H	Cl	H	H	CSSMe	Me	Me
A-54	OMe	Cl	H	H	H	CSSMe	Me	Me
A-55	OMe	H	Cl	H	H	CSSMe	Me	Me
A-56	OMe	Me	H	H	H	CSSMe	Me	Me
A-57	OMe	Et	H	H	H	CSSMe	Me	Me
A-58	OMe	H	Et	H	H	CSSMe	Me	Me
A-59	OMe	H	Pr^i	H	H	CSSMe	Me	Me
A-60	OMe	H	OEt	H	H	CSSMe	Me	Me
A-61	OMe	H	OPr	H	H	CSSMe	Me	Me
A-62	OMe	NMe_2	H	H	H	CSSMe	Me	Me
A-63	OMe	NEt_2	H	H	H	CSSMe	Me	Me
A-64	OEt	NMe_2	H	H	H	CSSMe	Me	Me
A-65	OEt	NEt_2	H	H	H	CSSMe	Me	Me
A-66	H	OMe	F	H	H	CSSMe	Me	Me
A-67	H	OMe	Cl	H	H	CSSMe	Me	Me
A-68	H	OMe	OPr^i	H	H	CSSMe	Me	Me
A-69	H	OEt	OPr	H	H	CSSMe	Me	Me
A-70	H	OEt	OPr^i	H	H	CSSMe	Me	Me
A-71	H	OEt	OBu	H	H	CSSMe	Me	Me
A-72	SMe	SMe	H	H	H	CSSMe	Me	Me
A-73	SMe	H	SMe	H	H	CSSMe	Me	Me
A-74	NMe_2	NMe_2	H	H	H	CSSMe	Me	Me
A-75	NMe_2	H	NMe_2	H	H	CSSMe	Me	Me

(Table 42)



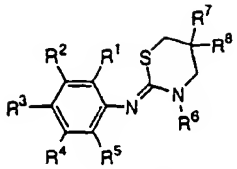
	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
B-1	H	H	H	H	H	COSMe	Me	Me
B-2	Cl	H	H	H	H	COSMe	Me	Me
B-3	Br	H	H	H	H	COSMe	Me	Me
B-4	Me	H	H	H	H	COSMe	Me	Me
B-5	Et	H	H	H	H	COSMe	Me	Me
B-6	Bu	H	H	H	H	COSMe	Me	Me
B-7	Bu^i	H	H	H	H	COSMe	Me	Me
B-8	Bu^t	H	H	H	H	COSMe	Me	Me
B-9	OEt	H	H	H	H	COSMe	Me	Me
B-10	OPr	H	H	H	H	COSMe	Me	Me
B-11	$OCHF_2$	H	H	H	H	COSMe	Me	Me
B-12	OCF_3	H	H	H	H	COSMe	Me	Me
B-13	CF_3	H	H	H	H	COSMe	Me	Me
B-14	SMe	H	H	H	H	COSMe	Me	Me
B-15	SEt	H	H	H	H	COSMe	Me	Me
B-16	SPr^i	H	H	H	H	COSMe	Me	Me
B-17	NMe_2	H	H	H	H	COSMe	Me	Me
B-18	NEt_2	H	H	H	H	COSMe	Me	Me
B-19	H	Cl	H	H	H	COSMe	Me	Me
B-20	H	Br	H	H	H	COSMe	Me	Me
B-21	H	Me	H	H	H	COSMe	Me	Me
B-22	H	Et	H	H	H	COSMe	Me	Me
B-23	H	Pr	H	H	H	COSMe	Me	Me
B-24	H	Bu	H	H	H	COSMe	Me	Me
B-25	H	Bu^i	H	H	H	COSMe	Me	Me

(Table 43)



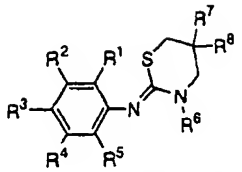
	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
B-26	H	Bu^s	H	H	H	COSMe	Me	Me
B-27	H	Bu^t	H	H	H	COSMe	Me	Me
B-28	H	OMe	H	H	H	COSMe	Me	Me
B-29	H	OEt	H	H	H	COSMe	Me	Me
B-30	H	OPr	H	H	H	COSMe	Me	Me
B-31	H	$OCHF_2$	H	H	H	COSMe	Me	Me
B-32	H	OCF_3	H	H	H	COSMe	Me	Me
B-33	H	CF_3	H	H	H	COSMe	Me	Me
B-34	H	SMe	H	H	H	COSMe	Me	Me
B-35	H	SEt	H	H	H	COSMe	Me	Me
B-36	H	SPr^i	H	H	H	COSMe	Me	Me
B-37	H	NMe_2	H	H	H	COSMe	Me	Me
B-38	H	NEt_2	H	H	H	COSMe	Me	Me
B-39	H	H	Cl	H	H	COSMe	Me	Me
B-40	H	H	Br	H	H	COSMe	Me	Me
B-41	H	H	Me	H	H	COSMe	Me	Me
B-42	H	H	Pr	H	H	COSMe	Me	Me
B-43	H	H	Bu	H	H	COSMe	Me	Me
B-44	H	H	Bu^i	H	H	COSMe	Me	Me
B-45	H	H	Bu^s	H	H	COSMe	Me	Me
B-46	H	H	Bu^t	H	H	COSMe	Me	Me
B-47	H	H	OMe	H	H	COSMe	Me	Me
B-48	H	H	OEt	H	H	COSMe	Me	Me
B-49	H	H	OPr	H	H	COSMe	Me	Me
B-50	H	H	$OCHF_2$	H	H	COSMe	Me	Me

(Table 44)



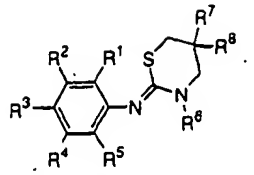
	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
B-51	H	H	OCF_3	H	H	COSMe	Me	Me
B-52	H	H	CF_3	H	H	COSMe	Me	Me
B-53	H	H	SMe	H	H	COSMe	Me	Me
B-54	H	H	SEt	H	H	COSMe	Me	Me
B-55	H	H	SPr^i	H	H	COSMe	Me	Me
B-56	H	H	NMe_2	H	H	COSMe	Me	Me
B-57	H	H	NEt_2	H	H	COSMe	Me	Me
B-58	Me	Me	H	H	H	COSMe	Me	Me
B-59	H	Me	Me	H	H	COSMe	Me	Me
B-60	Et	Et	H	H	H	COSMe	Me	Me
B-61	H	Et	Et	H	H	COSMe	Me	Me
B-62	OMe	Me	H	H	H	COSMe	Me	Me
B-63	OMe	H	Me	H	H	COSMe	Me	Me
B-64	NMe_2	Me	H	H	H	COSMe	Me	Me
B-65	H	NMe_2	Me	H	H	COSMe	Me	Me
B-66	Me	NMe_2	H	H	H	COSMe	Me	Me
B-67	NMe_2	Cl	H	H	H	COSMe	Me	Me
B-68	Me	NEt_2	H	H	H	COSMe	Me	Me
B-69	H	NEt_2	Me	H	H	COSMe	Me	Me
B-70	Pr^i	H	F	H	H	COSMe	Me	Me

(Table 45)



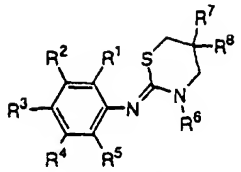
	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
C-1	H	H	H	H	H	CSSEt	Me	Me
C-2	Cl	H	H	H	H	CSSEt	Me	Me
C-3	Br	H	H	H	H	CSSEt	Me	Me
C-4	Me	H	H	H	H	CSSEt	Me	Me
C-5	Et	H	H	H	H	CSSEt	Me	Me
C-6	Pr	H	H	H	H	CSSEt	Me	Me
C-7	Bu	H	H	H	H	CSSEt	Me	Me
C-8	Bu^i	H	H	H	H	CSSEt	Me	Me
C-9	Bu^t	H	H	H	H	CSSEt	Me	Me
C-10	OMe	H	H	H	H	CSSEt	Me	Me
C-11	OPr	H	H	H	H	CSSEt	Me	Me
C-12	$OCHF_2$	H	H	H	H	CSSEt	Me	Me
C-13	OCF_3	H	H	H	H	CSSEt	Me	Me
C-14	CF_3	H	H	H	H	CSSEt	Me	Me
C-15	SEt	H	H	H	H	CSSEt	Me	Me
C-16	SPr^i	H	H	H	H	CSSEt	Me	Me
C-17	NEt_2	H	H	H	H	CSSEt	Me	Me
C-18	H	Cl	H	H	H	CSSEt	Me	Me
C-19	H	Br	H	H	H	CSSEt	Me	Me
C-20	H	Me	H	H	H	CSSEt	Me	Me
C-21	H	Et	H	H	H	CSSEt	Me	Me
C-22	H	Pr	H	H	H	CSSEt	Me	Me
C-23	H	Bu	H	H	H	CSSEt	Me	Me
C-24	H	Bu^i	H	H	H	CSSEt	Me	Me
C-25	H	Bu^s	H	H	H	CSSEt	Me	Me

(Table 46)



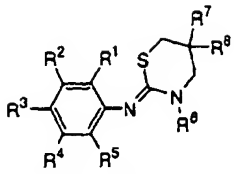
	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
C-26	H	Bu^t	H	H	H	CSSEt	Me	Me
C-27	H	OMe	H	H	H	CSSEt	Me	Me
C-28	H	OEt	H	H	H	CSSEt	Me	Me
C-29	H	OPr	H	H	H	CSSEt	Me	Me
C-30	H	$OCHF_2$	H	H	H	CSSEt	Me	Me
C-31	H	OCF_3	H	H	H	CSSEt	Me	Me
C-32	H	CF_3	H	H	H	CSSEt	Me	Me
C-33	H	SMe	H	H	H	CSSEt	Me	Me
C-34	H	SEt	H	H	H	CSSEt	Me	Me
C-35	H	SPr^i	H	H	H	CSSEt	Me	Me
C-36	H	NEt_2	H	H	H	CSSEt	Me	Me
C-37	H	H	Cl	H	H	CSSEt	Me	Me
C-38	H	H	Br	H	H	CSSEt	Me	Me
C-39	H	H	Me	H	H	CSSEt	Me	Me
C-40	H	H	Et	H	H	CSSEt	Me	Me
C-41	H	H	Pr	H	H	CSSEt	Me	Me
C-42	H	H	Bu	H	H	CSSEt	Me	Me
C-43	H	H	Bu^i	H	H	CSSEt	Me	Me
C-44	H	H	Bu^s	H	H	CSSEt	Me	Me
C-45	H	H	Bu^t	H	H	CSSEt	Me	Me
C-46	H	H	OMe	H	H	CSSEt	Me	Me
C-47	H	H	OEt	H	H	CSSEt	Me	Me
C-48	H	H	OPr	H	H	CSSEt	Me	Me
C-49	H	H	$OCHF_2$	H	H	CSSEt	Me	Me
C-50	H	H	OCF_3	H	H	CSSEt	Me	Me

(Table 47)



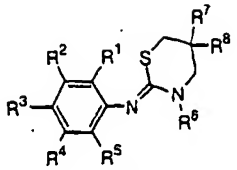
	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
C-51	H	H	CF_3	H	H	CSSEt	Me	Me
C-52	H	H	SMe	H	H	CSSEt	Me	Me
C-53	H	H	SEt	H	H	CSSEt	Me	Me
C-54	H	H	SPr^i	H	H	CSSEt	Me	Me
C-55	H	H	NMe_2	H	H	CSSEt	Me	Me
C-56	H	H	NEt_2	H	H	CSSEt	Me	Me
C-57	Me	Me	H	H	H	CSSEt	Me	Me
C-58	H	Me	Me	H	H	CSSEt	Me	Me
C-59	Et	Et	H	H	H	CSSEt	Me	Me
C-60	H	Et	Et	H	H	CSSEt	Me	Me
C-61	OMe	Me	H	H	H	CSSEt	Me	Me
C-62	OMe	H	Me	H	H	CSSEt	Me	Me
C-63	NMe_2	Me	H	H	H	CSSEt	Me	Me
C-64	H	NMe_2	Me	H	H	CSSEt	Me	Me
C-65	Me	NMe_2	H	H	H	CSSEt	Me	Me
C-66	NMe_2	Cl	H	H	H	CSSEt	Me	Me
C-67	Me	NEt_2	H	H	H	CSSEt	Me	Me
C-68	H	NEt_2	Me	H	H	CSSEt	Me	Me
C-69	Pr^i	H	F	H	H	CSSEt	Me	Me
C-70	OMe	H	OMe	H	H	CSSEt	Me	Me
C-71	H	OMe	OMe	H	H	CSSEt	Me	Me
C-72	H	OMe	OEt	H	H	CSSEt	Me	Me
C-73	H	OEt	OMe	H	H	CSSEt	Me	Me
C-74	H	OEt	OEt	H	H	CSSEt	Me	Me
C-75	OMe	H	Me	H	H	CSSEt	Me	Me

(Table 48)



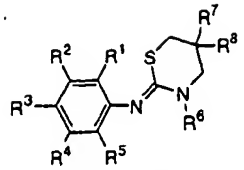
	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
D-1	Br	H	H	H	H	COSEt	Me	Me
D-2	Bu^i	H	H	H	H	COSEt	Me	Me
D-3	OPr	H	H	H	H	COSEt	Me	Me
D-4	$OCHF_2$	H	H	H	H	COSEt	Me	Me
D-5	OCF_3	H	H	H	H	COSEt	Me	Me
D-6	NEt_2	H	H	H	H	COSEt	Me	Me
D-7	H	Cl	H	H	H	COSEt	Me	Me
D-8	H	Br	H	H	H	COSEt	Me	Me
D-9	H	Et	H	H	H	COSEt	Me	Me
D-10	H	Pr	H	H	H	COSEt	Me	Me
D-11	H	Bu	H	H	H	COSEt	Me	Me
D-12	H	Bu^i	H	H	H	COSEt	Me	Me
D-13	H	Bu^s	H	H	H	COSEt	Me	Me
D-14	H	Bu^t	H	H	H	COSEt	Me	Me
D-15	H	OEt	H	H	H	COSEt	Me	Me
D-16	H	OPr	H	H	H	COSEt	Me	Me
D-17	H	$OCHF_2$	H	H	H	COSEt	Me	Me
D-18	H	OCF_3	H	H	H	COSEt	Me	Me
D-19	H	CF_3	H	H	H	COSEt	Me	Me
D-20	H	SMe	H	H	H	COSEt	Me	Me
D-21	H	SEt	H	H	H	COSEt	Me	Me
D-22	H	SPr^i	H	H	H	COSEt	Me	Me
D-23	H	NMe_2	H	H	H	COSEt	Me	Me
D-24	H	NEt_2	H	H	H	COSEt	Me	Me
D-25	H	H	Br	H	H	COSEt	Me	Me

(Table 49)



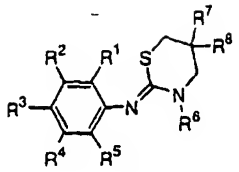
	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
D-26	H	H	Et	H	H	COSEt	Me	Me
D-27	H	H	Pr	H	H	COSEt	Me	Me
D-28	H	H	Bu	H	H	COSEt	Me	Me
D-29	H	H	Bu^i	H	H	COSEt	Me	Me
D-30	H	H	Bu^s	H	H	COSEt	Me	Me
D-31	H	H	Bu^t	H	H	COSEt	Me	Me
D-32	H	H	OMe	H	H	COSEt	Me	Me
D-33	H	H	OEt	H	H	COSEt	Me	Me
D-34	H	H	OPr	H	H	COSEt	Me	Me
D-35	H	H	$OCHF_2$	H	H	COSEt	Me	Me
D-36	H	H	OCF_3	H	H	COSEt	Me	Me
D-37	H	H	CF_3	H	H	COSEt	Me	Me
D-38	H	H	SMe	H	H	COSEt	Me	Me
D-39	H	H	SEt	H	H	COSEt	Me	Me
D-40	H	H	SPr^i	H	H	COSEt	Me	Me
D-41	H	H	NMe_2	H	H	COSEt	Me	Me
D-42	H	H	NEt_2	H	H	COSEt	Me	Me
D-43	Et	Et	H	H	H	COSEt	Me	Me
D-44	H	Et	Et	H	H	COSEt	Me	Me
D-45	OMe	Me	H	H	H	COSEt	Me	Me
D-46	OMe	H	Me	H	H	COSEt	Me	Me
D-47	NMe_2	Me	H	H	H	COSEt	Me	Me
D-48	H	NMe_2	Me	H	H	COSEt	Me	Me
D-49	H	OEt	OMe	H	H	COSEt	Me	Me
D-50	H	OEt	OEt	H	H	COSEt	Me	Me

(Table 50)



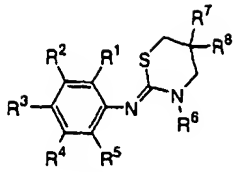
	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
E-1	H	H	H	H	H	CSSMe	Et	Et
E-2	Cl	H	H	H	H	CSSMe	Et	Et
E-3	Br	H	H	H	H	CSSMe	Et	Et
E-4	Me	H	H	H	H	CSSMe	Et	Et
E-5	Et	H	H	H	H	CSSMe	Et	Et
E-6	Pr	H	H	H	H	CSSMe	Et	Et
E-7	Bu	H	H	H	H	CSSMe	Et	Et
E-8	Bu'	H	H	H	H	CSSMe	Et	Et
E-9	Bu'	H	H	H	H	CSSMe	Et	Et
E-10	OMe	H	H	H	H	CSSMe	Et	Et
E-11	OEt	H	H	H	H	CSSMe	Et	Et
E-12	OPr'	H	H	H	H	CSSMe	Et	Et
E-13	OPr	H	H	H	H	CSSMe	Et	Et
E-14	$OCHF_2$	H	H	H	H	CSSMe	Et	Et
E-15	OCF_3	H	H	H	H	CSSMe	Et	Et
E-16	CF_3	H	H	H	H	CSSMe	Et	Et
E-17	SMe	H	H	H	H	CSSMe	Et	Et
E-18	SEt	H	H	H	H	CSSMe	Et	Et
E-19	SPr'	H	H	H	H	CSSMe	Et	Et
E-20	NMe_2	H	H	H	H	CSSMe	Et	Et
E-21	NEt_2	H	H	H	H	CSSMe	Et	Et
E-22	H	Cl	H	H	H	CSSMe	Et	Et
E-23	H	Br	H	H	H	CSSMe	Et	Et
E-24	H	Me	H	H	H	CSSMe	Et	Et
E-25	H	Et	H	H	H	CSSMe	Et	Et

(Table 51)



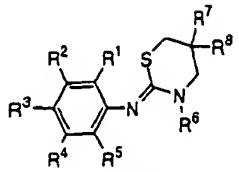
	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
E-26	H	Pr	H	H	H	CSSMe	Et	Et
E-27	H	Pr^i	H	H	H	CSSMe	Et	Et
E-28	H	Bu	H	H	H	CSSMe	Et	Et
E-29	H	Bu^i	H	H	H	CSSMe	Et	Et
E-30	H	Bu^s	H	H	H	CSSMe	Et	Et
E-31	H	Bu^t	H	H	H	CSSMe	Et	Et
E-32	H	OMe	H	H	H	CSSMe	Et	Et
E-33	H	OEt	H	H	H	CSSMe	Et	Et
E-34	H	OPr	H	H	H	CSSMe	Et	Et
E-35	H	OPr^i	H	H	H	CSSMe	Et	Et
E-36	H	$OCHF_2$	H	H	H	CSSMe	Et	Et
E-37	H	OCF_3	H	H	H	CSSMe	Et	Et
E-38	H	CF_3	H	H	H	CSSMe	Et	Et
E-39	H	SMe	H	H	H	CSSMe	Et	Et
E-40	H	SEt	H	H	H	CSSMe	Et	Et
E-41	H	SPr^i	H	H	H	CSSMe	Et	Et
E-42	H	NMe_2	H	H	H	CSSMe	Et	Et
E-43	H	NEt_2	H	H	H	CSSMe	Et	Et
E-44	H	H	Cl	H	H	CSSMe	Et	Et
E-45	H	H	Br	H	H	CSSMe	Et	Et
E-46	H	H	Me	H	H	CSSMe	Et	Et
E-47	H	H	Et	H	H	CSSMe	Et	Et
E-48	H	H	Pr	H	H	CSSMe	Et	Et
E-49	H	H	Pr^i	H	H	CSSMe	Et	Et
E-50	H	H	Bu	H	H	CSSMe	Et	Et

(Table 52)



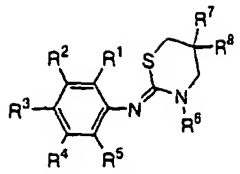
	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
E-51	H	H	Bu^i	H	H	CSSMe	Et	Et
E-52	H	H	Bu^s	H	H	CSSMe	Et	Et
E-53	H	H	Bu^t	H	H	CSSMe	Et	Et
E-54	H	H	OMe	H	H	CSSMe	Et	Et
E-55	H	H	OEt	H	H	CSSMe	Et	Et
E-56	H	H	OPr	H	H	CSSMe	Et	Et
E-57	H	H	OPr^i	H	H	CSSMe	Et	Et
E-58	H	H	$OCHF_2$	H	H	CSSMe	Et	Et
E-59	H	H	OCF_3	H	H	CSSMe	Et	Et
E-60	H	H	CF_3	H	H	CSSMe	Et	Et
E-61	H	H	SMe	H	H	CSSMe	Et	Et
E-62	H	H	SEt	H	H	CSSMe	Et	Et
E-63	H	H	SPr^i	H	H	CSSMe	Et	Et
E-64	H	H	NMe_2	H	H	CSSMe	Et	Et
E-65	H	H	NEt_2	H	H	CSSMe	Et	Et
E-66	Me	NMe_2	H	H	H	CSSMe	Et	Et
E-67	NMe_2	Cl	H	H	H	CSSMe	Et	Et
E-68	Me	NEt_2	H	H	H	CSSMe	Et	Et
E-69	H	NEt_2	Me	H	H	CSSMe	Et	Et
E-70	Pr^i	H	F	H	H	CSSMe	Et	Et
E-71	OMe	H	OMe	H	H	CSSMe	Et	Et
E-72	H	OMe	OMe	H	H	CSSMe	Et	Et
E-73	H	OMe	OEt	H	H	CSSMe	Et	Et
E-74	H	OEt	OMe	H	H	CSSMe	Et	Et
E-75	H	OEt	OEt	H	H	CSSMe	Et	Et

(Table 53)



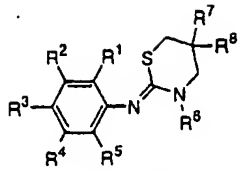
	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
F-1	H	H	H	H	H	CSSMe	Pr	Pr
F-2	Cl	H	H	H	H	CSSMe	Pr	Pr
F-3	Br	H	H	H	H	CSSMe	Pr	Pr
F-4	Me	H	H	H	H	CSSMe	Pr	Pr
F-5	Et	H	H	H	H	CSSMe	Pr	Pr
F-6	Pr	H	H	H	H	CSSMe	Pr	Pr
F-7	Bu	H	H	H	H	CSSMe	Pr	Pr
F-8	Bu'	H	H	H	H	CSSMe	Pr	Pr
F-9	Bu^t	H	H	H	H	CSSMe	Pr	Pr
F-10	OMe	H	H	H	H	CSSMe	Pr	Pr
F-11	OEt	H	H	H	H	CSSMe	Pr	Pr
F-12	OPr'	H	H	H	H	CSSMe	Pr	Pr
F-13	OPr	H	H	H	H	CSSMe	Pr	Pr
F-14	$OCHF_2$	H	H	H	H	CSSMe	Pr	Pr
F-15	OCF_3	H	H	H	H	CSSMe	Pr	Pr
F-16	CF_3	H	H	H	H	CSSMe	Pr	Pr
F-17	SMe	H	H	H	H	CSSMe	Pr	Pr
F-18	SEt	H	H	H	H	CSSMe	Pr	Pr
F-19	SPr'	H	H	H	H	CSSMe	Pr	Pr
F-20	NMe_2	H	H	H	H	CSSMe	Pr	Pr
F-21	NEt_2	H	H	H	H	CSSMe	Pr	Pr
F-22	H	Cl	H	H	H	CSSMe	Pr	Pr
F-23	H	Br	H	H	H	CSSMe	Pr	Pr
F-24	H	Me	H	H	H	CSSMe	Pr	Pr
F-25	H	Et	H	H	H	CSSMe	Pr	Pr

(Table 54)



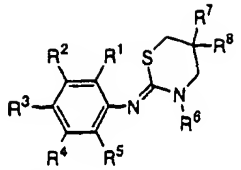
	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
F-26	H	Pr	H	H	H	CSSMe	Pr	Pr
F-27	H	Pr^i	H	H	H	CSSMe	Pr	Pr
F-28	H	Bu	H	H	H	CSSMe	Pr	Pr
F-29	H	Bu^i	H	H	H	CSSMe	Pr	Pr
F-30	H	Bu^s	H	H	H	CSSMe	Pr	Pr
F-31	H	Bu^t	H	H	H	CSSMe	Pr	Pr
F-32	H	OMe	H	H	H	CSSMe	Pr	Pr
F-33	H	OEt	H	H	H	CSSMe	Pr	Pr
F-34	H	OPr	H	H	H	CSSMe	Pr	Pr
F-35	H	OPr^i	H	H	H	CSSMe	Pr	Pr
F-36	H	$OCHF_2$	H	H	H	CSSMe	Pr	Pr
F-37	H	OCF_3	H	H	H	CSSMe	Pr	Pr
F-38	H	CF_3	H	H	H	CSSMe	Pr	Pr
F-39	H	SMe	H	H	H	CSSMe	Pr	Pr
F-40	H	SEt	H	H	H	CSSMe	Pr	Pr
F-41	H	SPr^i	H	H	H	CSSMe	Pr	Pr
F-42	H	NMe_2	H	H	H	CSSMe	Pr	Pr
F-43	H	NEt_2	H	H	H	CSSMe	Pr	Pr
F-44	H	H	Cl	H	H	CSSMe	Pr	Pr
F-45	H	H	Br	H	H	CSSMe	Pr	Pr
F-46	H	H	Me	H	H	CSSMe	Pr	Pr
F-47	H	H	Et	H	H	CSSMe	Pr	Pr
F-48	H	H	Pr	H	H	CSSMe	Pr	Pr
F-49	H	H	Pr^i	H	H	CSSMe	Pr	Pr
F-50	H	H	Bu	H	H	CSSMe	Pr	Pr

(Table 55)



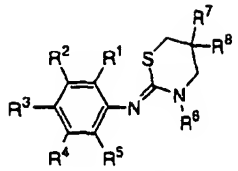
	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
F-51	H	H	Bu^i	H	H	CSSMe	Pr	Pr
F-52	H	H	Bu^s	H	H	CSSMe	Pr	Pr
F-53	H	H	Bu^t	H	H	CSSMe	Pr	Pr
F-54	H	H	OMe	H	H	CSSMe	Pr	Pr
F-55	H	H	OEt	H	H	CSSMe	Pr	Pr
F-56	H	H	OPr	H	H	CSSMe	Pr	Pr
F-57	H	H	OPr^i	H	H	CSSMe	Pr	Pr
F-58	H	H	$OCHF_2$	H	H	CSSMe	Pr	Pr
F-59	H	H	OCF_3	H	H	CSSMe	Pr	Pr
F-60	H	H	CF_3	H	H	CSSMe	Pr	Pr
F-61	H	H	SMe	H	H	CSSMe	Pr	Pr
F-62	H	H	SEt	H	H	CSSMe	Pr	Pr
F-63	H	H	SPr^i	H	H	CSSMe	Pr	Pr
F-64	H	H	NMe_2	H	H	CSSMe	Pr	Pr
F-65	H	H	NEt_2	H	H	CSSMe	Pr	Pr
F-66	Me	NMe_2	H	H	H	CSSMe	Pr	Pr
F-67	NMe_2	Cl	H	H	H	CSSMe	Pr	Pr
F-68	Me	NEt_2	H	H	H	CSSMe	Pr	Pr
F-69	H	NEt_2	Me	H	H	CSSMe	Pr	Pr
F-70	Bu^s	H	H	H	H	CSSMe	Pr	Pr
F-71	OMe	H	OMe	H	H	CSSMe	Pr	Pr
F-72	H	OMe	OMe	H	H	CSSMe	Pr	Pr
F-73	H	OMe	OEt	H	H	CSSMe	Pr	Pr
F-74	H	OEt	OMe	H	H	CSSMe	Pr	Pr
F-75	H	OEt	OEt	H	H	CSSMe	Pr	Pr

(Table 56)



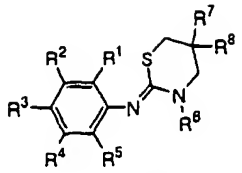
	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
G-1	H	H	H	H	H	CSSEt	Et	Et
G-2	Cl	H	H	H	H	CSSEt	Et	Et
G-3	Br	H	H	H	H	CSSEt	Et	Et
G-4	Me	H	H	H	H	CSSEt	Et	Et
G-5	Et	H	H	H	H	CSSEt	Et	Et
G-6	Pr	H	H	H	H	CSSEt	Et	Et
G-7	Bu	H	H	H	H	CSSEt	Et	Et
G-8	Bu'	H	H	H	H	CSSEt	Et	Et
G-9	Bu'	H	H	H	H	CSSEt	Et	Et
G-10	OMe	H	H	H	H	CSSEt	Et	Et
G-11	OEt	H	H	H	H	CSSEt	Et	Et
G-12	OPr'	H	H	H	H	CSSEt	Et	Et
G-13	OPr	H	H	H	H	CSSEt	Et	Et
G-14	$OCHF_2$	H	H	H	H	CSSEt	Et	Et
G-15	OCF_3	H	H	H	H	CSSEt	Et	Et
G-16	CF_3	H	H	H	H	CSSEt	Et	Et
G-17	SMe	H	H	H	H	CSSEt	Et	Et
G-18	SEt	H	H	H	H	CSSEt	Et	Et
G-19	SPr'	H	H	H	H	CSSEt	Et	Et
G-20	NMe_2	H	H	H	H	CSSEt	Et	Et
G-21	NEt_2	H	H	H	H	CSSEt	Et	Et
G-22	H	Cl	H	H	H	CSSEt	Et	Et
G-23	H	Br	H	H	H	CSSEt	Et	Et
G-24	H	Me	H	H	H	CSSEt	Et	Et
G-25	H	Et	H	H	H	CSSEt	Et	Et

(Table 57)



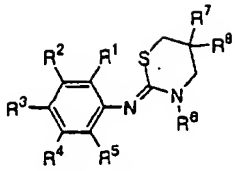
	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
G-26	H	Pr	H	H	H	CSSEt	Et	Et
G-27	H	Pr^i	H	H	H	CSSEt	Et	Et
G-28	H	Bu	H	H	H	CSSEt	Et	Et
G-29	H	Bu^i	H	H	H	CSSEt	Et	Et
G-30	H	Bu^s	H	H	H	CSSEt	Et	Et
G-31	H	Bu^t	H	H	H	CSSEt	Et	Et
G-32	H	OMe	H	H	H	CSSEt	Et	Et
G-33	H	OEt	H	H	H	CSSEt	Et	Et
G-34	H	OPr	H	H	H	CSSEt	Et	Et
G-35	H	OPr^i	H	H	H	CSSEt	Et	Et
G-36	H	$OCHF_2$	H	H	H	CSSEt	Et	Et
G-37	H	OCF_3	H	H	H	CSSEt	Et	Et
G-38	H	CF_3	H	H	H	CSSEt	Et	Et
G-39	H	SMe	H	H	H	CSSEt	Et	Et
G-40	H	SEt	H	H	H	CSSEt	Et	Et
G-41	H	SPr^i	H	H	H	CSSEt	Et	Et
G-42	H	NMe_2	H	H	H	CSSEt	Et	Et
G-43	H	NEt_2	H	H	H	CSSEt	Et	Et
G-44	H	H	Cl	H	H	CSSEt	Et	Et
G-45	H	H	Br	H	H	CSSEt	Et	Et
G-46	H	H	Me	H	H	CSSEt	Et	Et
G-47	H	H	Et	H	H	CSSEt	Et	Et
G-48	H	H	Pr	H	H	CSSEt	Et	Et
G-49	H	H	Pr^i	H	H	CSSEt	Et	Et
G-50	H	H	Bu	H	H	CSSEt	Et	Et

(Table 58)



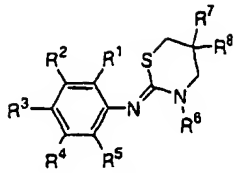
	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
G-51	H	H	Bu^i	H	H	CSSEt	Et	Et
G-52	H	H	Bu^s	H	H	CSSEt	Et	Et
G-53	H	H	Bu^t	H	H	CSSEt	Et	Et
G-54	H	H	OMe	H	H	CSSEt	Et	Et
G-55	H	H	OEt	H	H	CSSEt	Et	Et
G-56	H	H	OPr	H	H	CSSEt	Et	Et
G-57	H	H	OPr^i	H	H	CSSEt	Et	Et
G-58	H	H	$OCHF_2$	H	H	CSSEt	Et	Et
G-59	H	H	OCF_3	H	H	CSSEt	Et	Et
G-60	H	H	CF_3	H	H	CSSEt	Et	Et
G-61	H	H	SMe	H	H	CSSEt	Et	Et
G-62	H	H	SEt	H	H	CSSEt	Et	Et
G-63	H	H	SPr^i	H	H	CSSEt	Et	Et
G-64	H	H	NMe_2	H	H	CSSEt	Et	Et
G-65	H	H	NEt_2	H	H	CSSEt	Et	Et
G-66	Me	NMe_2	H	H	H	CSSEt	Et	Et
G-67	NMe_2	Cl	H	H	H	CSSEt	Et	Et
G-68	Me	NEt_2	H	H	H	CSSEt	Et	Et
G-69	H	NEt_2	Me	H	H	CSSEt	Et	Et
G-70	Bu^s	H	H	H	H	CSSEt	Et	Et
G-71	OMe	H	OMe	H	H	CSSEt	Et	Et
G-72	H	OMe	OMe	H	H	CSSEt	Et	Et
G-73	H	OMe	OEt	H	H	CSSEt	Et	Et
G-74	H	OEt	OMe	H	H	CSSEt	Et	Et
G-75	H	OEt	OEt	H	H	CSSEt	Et	Et

(Table 59)



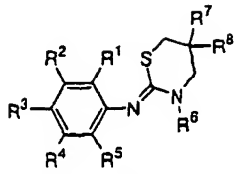
	R^1	R^2	R^3	R^4	R^5	R^6	R^7 R^8
H-1	H	H	H	H	H	CSSMe	$-(CH_2)_2-$
H-2	Cl	H	H	H	H	CSSMe	$-(CH_2)_2-$
H-3	Br	H	H	H	H	CSSMe	$-(CH_2)_2-$
H-4	Me	H	H	H	H	CSSMe	$-(CH_2)_2-$
H-5	Et	H	H	H	H	CSSMe	$-(CH_2)_2-$
H-6	Pr	H	H	H	H	CSSMe	$-(CH_2)_2-$
H-7	Bu	H	H	H	H	CSSMe	$-(CH_2)_2-$
H-8	Bu^i	H	H	H	H	CSSMe	$-(CH_2)_2-$
H-9	Bu^t	H	H	H	H	CSSMe	$-(CH_2)_2-$
H-10	OMe	H	H	H	H	CSSMe	$-(CH_2)_2-$
H-11	OEt	H	H	H	H	CSSMe	$-(CH_2)_2-$
H-12	OPr^i	H	H	H	H	CSSMe	$-(CH_2)_2-$
H-13	OPr	H	H	H	H	CSSMe	$-(CH_2)_2-$
H-14	$OCHF_2$	H	H	H	H	CSSMe	$-(CH_2)_2-$
H-15	OCF_3	H	H	H	H	CSSMe	$-(CH_2)_2-$
H-16	CF_3	H	H	H	H	CSSMe	$-(CH_2)_2-$
H-17	SMe	H	H	H	H	CSSMe	$-(CH_2)_2-$
H-18	SEt	H	H	H	H	CSSMe	$-(CH_2)_2-$
H-19	SPr^i	H	H	H	H	CSSMe	$-(CH_2)_2-$
H-20	NMe_2	H	H	H	H	CSSMe	$-(CH_2)_2-$
H-21	NEt_2	H	H	H	H	CSSMe	$-(CH_2)_2-$
H-22	H	Cl	H	H	H	CSSMe	$-(CH_2)_2-$
H-23	H	Br	H	H	H	CSSMe	$-(CH_2)_2-$
H-24	H	Me	H	H	H	CSSMe	$-(CH_2)_2-$
H-25	H	Et	H	H	H	CSSMe	$-(CH_2)_2-$

(Table 60)



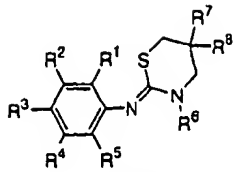
	R^1	R^2	R^3	R^4	R^5	R^6	R^7 R^8
H-26	H	Pr	H	H	H	CSSMe	-$(CH_2)_2$-
H-27	H	Pr^i	H	H	H	CSSMe	-$(CH_2)_2$-
H-28	H	Bu	H	H	H	CSSMe	-$(CH_2)_2$-
H-29	H	Bu^i	H	H	H	CSSMe	-$(CH_2)_2$-
H-30	H	Bu^s	H	H	H	CSSMe	-$(CH_2)_2$-
H-31	H	Bu^t	H	H	H	CSSMe	-$(CH_2)_2$-
H-32	H	OMe	H	H	H	CSSMe	-$(CH_2)_2$-
H-33	H	OEt	H	H	H	CSSMe	-$(CH_2)_2$-
H-34	H	OPr	H	H	H	CSSMe	-$(CH_2)_2$-
H-35	H	OPr^i	H	H	H	CSSMe	-$(CH_2)_2$-
H-36	H	$OCHF_2$	H	H	H	CSSMe	-$(CH_2)_2$-
H-37	H	OCF_3	H	H	H	CSSMe	-$(CH_2)_2$-
H-38	H	CF_3	H	H	H	CSSMe	-$(CH_2)_2$-
H-39	H	SMe	H	H	H	CSSMe	-$(CH_2)_2$-
H-40	H	SEt	H	H	H	CSSMe	-$(CH_2)_2$-
H-41	H	SPr^i	H	H	H	CSSMe	-$(CH_2)_2$-
H-42	H	NMe_2	H	H	H	CSSMe	-$(CH_2)_2$-
H-43	H	NEt_2	H	H	H	CSSMe	-$(CH_2)_2$-
H-44	H	H	Cl	H	H	CSSMe	-$(CH_2)_2$-
H-45	H	H	Br	H	H	CSSMe	-$(CH_2)_2$-
H-46	H	H	Me	H	H	CSSMe	-$(CH_2)_2$-
H-47	H	H	Et	H	H	CSSMe	-$(CH_2)_2$-
H-48	H	H	Pr	H	H	CSSMe	-$(CH_2)_2$-
H-49	H	H	Pr^i	H	H	CSSMe	-$(CH_2)_2$-
H-50	H	H	Bu	H	H	CSSMe	-$(CH_2)_2$-

(Table 61)



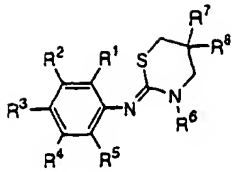
	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
H-51	H	H	Bu^i	H	H	CSSMe	$-(CH_2)_2-$	
H-52	H	H	Bu^s	H	H	CSSMe	$-(CH_2)_2-$	
H-53	H	H	Bu^t	H	H	CSSMe	$-(CH_2)_2-$	
H-54	H	H	OMe	H	H	CSSMe	$-(CH_2)_2-$	
H-55	H	H	OEt	H	H	CSSMe	$-(CH_2)_2-$	
H-56	H	H	OPr	H	H	CSSMe	$-(CH_2)_2-$	
H-57	H	H	OPr^i	H	H	CSSMe	$-(CH_2)_2-$	
H-58	H	H	$OCHF_2$	H	H	CSSMe	$-(CH_2)_2-$	
H-59	H	H	OCF_3	H	H	CSSMe	$-(CH_2)_2-$	
H-60	H	H	CF_3	H	H	CSSMe	$-(CH_2)_2-$	
H-61	H	H	SMe	H	H	CSSMe	$-(CH_2)_2-$	
H-62	H	H	SEt	H	H	CSSMe	$-(CH_2)_2-$	
H-63	H	H	SPr^i	H	H	CSSMe	$-(CH_2)_2-$	
H-64	H	H	NMe_2	H	H	CSSMe	$-(CH_2)_2-$	
H-65	H	H	NEt_2	H	H	CSSMe	$-(CH_2)_2-$	
H-66	Me	NMe_2	H	H	H	CSSMe	$-(CH_2)_2-$	
H-67	NMe_2	Cl	H	H	H	CSSMe	$-(CH_2)_2-$	
H-68	Me	NEt_2	H	H	H	CSSMe	$-(CH_2)_2-$	
H-69	H	NEt_2	Me	H	H	CSSMe	$-(CH_2)_2-$	
H-70	Bu^s	H	H	H	H	CSSMe	$-(CH_2)_2-$	
H-71	OMe	H	OMe	H	H	CSSMe	$-(CH_2)_2-$	
H-72	H	OMe	OMe	H	H	CSSMe	$-(CH_2)_2-$	
H-73	H	OMe	OEt	H	H	CSSMe	$-(CH_2)_2-$	
H-74	H	OEt	OMe	H	H	CSSMe	$-(CH_2)_2-$	
H-75	H	OEt	OEt	H	H	CSSMe	$-(CH_2)_2-$	

(Table 62)



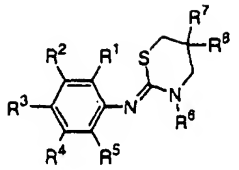
	R^1	R^2	R^3	R^4	R^5	R^6	R^7 R^8
N-1	H	H	H	H	H	CSSMe	-$(CH_2)_4$-
N-2	Cl	H	H	H	H	CSSMe	-$(CH_2)_4$-
N-3	Br	H	H	H	H	CSSMe	-$(CH_2)_4$-
N-4	Me	H	H	H	H	CSSMe	-$(CH_2)_4$-
N-5	Et	H	H	H	H	CSSMe	-$(CH_2)_4$-
N-6	Pr	H	H	H	H	CSSMe	-$(CH_2)_4$-
N-7	Bu	H	H	H	H	CSSMe	-$(CH_2)_4$-
N-8	Bu^i	H	H	H	H	CSSMe	-$(CH_2)_4$-
N-9	Bu^t	H	H	H	H	CSSMe	-$(CH_2)_4$-
N-10	OMe	H	H	H	H	CSSMe	-$(CH_2)_4$-
N-11	OEt	H	H	H	H	CSSMe	-$(CH_2)_4$-
N-12	OPr^i	H	H	H	H	CSSMe	-$(CH_2)_4$-
N-13	OPr	H	H	H	H	CSSMe	-$(CH_2)_4$-
N-14	$OCHF_2$	H	H	H	H	CSSMe	-$(CH_2)_4$-
N-15	OCF_3	H	H	H	H	CSSMe	-$(CH_2)_4$-
N-16	CF_3	H	H	H	H	CSSMe	-$(CH_2)_4$-
N-17	SMe	H	H	H	H	CSSMe	-$(CH_2)_4$-
N-18	SEt	H	H	H	H	CSSMe	-$(CH_2)_4$-
N-19	SPr^i	H	H	H	H	CSSMe	-$(CH_2)_4$-
N-20	NMe_2	H	H	H	H	CSSMe	-$(CH_2)_4$-
N-21	NEt_2	H	H	H	H	CSSMe	-$(CH_2)_4$-
N-22	H	Cl	H	H	H	CSSMe	-$(CH_2)_4$-
N-23	H	Br	H	H	H	CSSMe	-$(CH_2)_4$-
N-24	H	Me	H	H	H	CSSMe	-$(CH_2)_4$-
N-25	H	Et	H	H	H	CSSMe	-$(CH_2)_4$-

(Table 63)



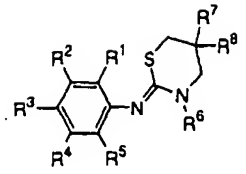
	R^1	R^2	R^3	R^4	R^5	R^6	R^7 R^8
N-26	H	Pr	H	H	H	CSSMe	-$(CH_2)_4$-
N-27	H	Pr^i	H	H	H	CSSMe	-$(CH_2)_4$-
N-28	H	Bu	H	H	H	CSSMe	-$(CH_2)_4$-
N-29	H	Bu^i	H	H	H	CSSMe	-$(CH_2)_4$-
N-30	H	Bu^s	H	H	H	CSSMe	-$(CH_2)_4$-
N-31	H	Bu^t	H	H	H	CSSMe	-$(CH_2)_4$-
N-32	H	OMe	H	H	H	CSSMe	-$(CH_2)_4$-
N-33	H	OEt	H	H	H	CSSMe	-$(CH_2)_4$-
N-34	H	OPr	H	H	H	CSSMe	-$(CH_2)_4$-
N-35	H	OPr^i	H	H	H	CSSMe	-$(CH_2)_4$-
N-36	H	$OCHF_2$	H	H	H	CSSMe	-$(CH_2)_4$-
N-37	H	OCF_3	H	H	H	CSSMe	-$(CH_2)_4$-
N-38	H	CF_3	H	H	H	CSSMe	-$(CH_2)_4$-
N-39	H	SMe	H	H	H	CSSMe	-$(CH_2)_4$-
N-40	H	SEt	H	H	H	CSSMe	-$(CH_2)_4$-
N-41	H	SPr^i	H	H	H	CSSMe	-$(CH_2)_4$-
N-42	H	NMe_2	H	H	H	CSSMe	-$(CH_2)_4$-
N-43	H	NEt_2	H	H	H	CSSMe	-$(CH_2)_4$-
N-44	H	H	Cl	H	H	CSSMe	-$(CH_2)_4$-
N-45	H	H	Br	H	H	CSSMe	-$(CH_2)_4$-
N-46	H	H	Me	H	H	CSSMe	-$(CH_2)_4$-
N-47	H	H	Et	H	H	CSSMe	-$(CH_2)_4$-
N-48	H	H	Pr	H	H	CSSMe	-$(CH_2)_4$-
N-49	H	H	Pr^i	H	H	CSSMe	-$(CH_2)_4$-
N-50	H	H	Bu	H	H	CSSMe	-$(CH_2)_4$-

(Table 64)



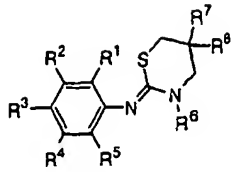
	R^1	R^2	R^3	R^4	R^5	$R^{6'}$	R^7 R^8
N-51	H	H	Bu^i	H	H	CSSMe	-$(CH_2)_4$-
N-52	H	H	Bu^s	H	H	CSSMe	-$(CH_2)_4$-
N-53	H	H	Bu^t	H	H	CSSMe	-$(CH_2)_4$-
N-54	H	H	OMe	H	H	CSSMe	-$(CH_2)_4$-
N-55	H	H	OEt	H	H	CSSMe	-$(CH_2)_4$-
N-56	H	H	OPr	H	H	CSSMe	-$(CH_2)_4$-
N-57	H	H	OPr^i	H	H	CSSMe	-$(CH_2)_4$-
N-58	H	H	$OCHF_2$	H	H	CSSMe	-$(CH_2)_4$-
N-59	H	H	OCF_3	H	H	CSSMe	-$(CH_2)_4$-
N-60	H	H	CF_3	H	H	CSSMe	-$(CH_2)_4$-
N-61	H	H	SMe	H	H	CSSMe	-$(CH_2)_4$-
N-62	H	H	SEt	H	H	CSSMe	-$(CH_2)_4$-
N-63	H	H	SPr^i	H	H	CSSMe	-$(CH_2)_4$-
N-64	H	H	NMe_2	H	H	CSSMe	-$(CH_2)_4$-
N-65	H	H	NEt_2	H	H	CSSMe	-$(CH_2)_4$-
N-66	Me	NMe_2	H	H	H	CSSMe	-$(CH_2)_4$-
N-67	NMe_2	Cl	H	H	H	CSSMe	-$(CH_2)_4$-
N-68	Me	NEt_2	H	H	H	CSSMe	-$(CH_2)_4$-
N-69	H	NEt_2	Me	H	H	CSSMe	-$(CH_2)_4$-
N-70	Bu^s	H	H	H	H	CSSMe	-$(CH_2)_4$-
N-71	OMe	H	OMe	H	H	CSSMe	-$(CH_2)_4$-
N-72	H	OMe	OMe	H	H	CSSMe	-$(CH_2)_4$-
N-73	H	OMe	OEt	H	H	CSSMe	-$(CH_2)_4$-
N-74	H	OEt	OMe	H	H	CSSMe	-$(CH_2)_4$-
N-75	H	OEt	OEt	H	H	CSSMe	-$(CH_2)_4$-

(Table 65)



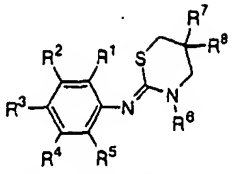
	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
J-1	H	H	H	H	H	CSSMe	$-(CH_2)_5-$	
J-2	Cl	H	H	H	H	CSSMe	$-(CH_2)_5-$	
J-3	Br	H	H	H	H	CSSMe	$-(CH_2)_5-$	
J-4	Me	H	H	H	H	CSSMe	$-(CH_2)_5-$	
J-5	Et	H	H	H	H	CSSMe	$-(CH_2)_5-$	
J-6	Pr	H	H	H	H	CSSMe	$-(CH_2)_5-$	
J-7	Bu	H	H	H	H	CSSMe	$-(CH_2)_5-$	
J-8	Bu'	H	H	H	H	CSSMe	$-(CH_2)_5-$	
J-9	Bu'	H	H	H	H	CSSMe	$-(CH_2)_5-$	
J-10	OMe	H	H	H	H	CSSMe	$-(CH_2)_5-$	
J-11	OEt	H	H	H	H	CSSMe	$-(CH_2)_5-$	
J-12	OPr'	H	H	H	H	CSSMe	$-(CH_2)_5-$	
J-13	OPr	H	H	H	H	CSSMe	$-(CH_2)_5-$	
J-14	$OCHF_2$	H	H	H	H	CSSMe	$-(CH_2)_5-$	
J-15	OCF_3	H	H	H	H	CSSMe	$-(CH_2)_5-$	
J-16	CF_3	H	H	H	H	CSSMe	$-(CH_2)_5-$	
J-17	SMe	H	H	H	H	CSSMe	$-(CH_2)_5-$	
J-18	SEt	H	H	H	H	CSSMe	$-(CH_2)_5-$	
J-19	SPr'	H	H	H	H	CSSMe	$-(CH_2)_5-$	
J-20	NMe_2	H	H	H	H	CSSMe	$-(CH_2)_5-$	
J-21	NEt_2	H	H	H	H	CSSMe	$-(CH_2)_5-$	
J-22	H	Cl	H	H	H	CSSMe	$-(CH_2)_5-$	
J-23	H	Br	H	H	H	CSSMe	$-(CH_2)_5-$	
J-24	H	Me	H	H	H	CSSMe	$-(CH_2)_5-$	
J-25	H	Et	H	H	H	CSSMe	$-(CH_2)_5-$	

(Table 66)



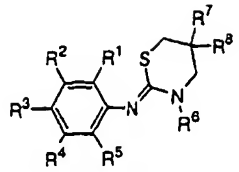
	R^1	R^2	R^3	R^4	R^5	R^6	R^7-R^8
J-26	H	Pr	H	H	H	CSSMe	-$(CH_2)_5$-
J-27	H	Pr^i	H	H	H	CSSMe	-$(CH_2)_5$-
J-28	H	Bu	H	H	H	CSSMe	-$(CH_2)_5$-
J-29	H	Bu^i	H	H	H	CSSMe	-$(CH_2)_5$-
J-30	H	Bu^s	H	H	H	CSSMe	-$(CH_2)_5$-
J-31	H	Bu^t	H	H	H	CSSMe	-$(CH_2)_5$-
J-32	H	OMe	H	H	H	CSSMe	-$(CH_2)_5$-
J-33	H	OEt	H	H	H	CSSMe	-$(CH_2)_5$-
J-34	H	OPr	H	H	H	CSSMe	-$(CH_2)_5$-
J-35	H	OPr^i	H	H	H	CSSMe	-$(CH_2)_5$-
J-36	H	$OCHF_2$	H	H	H	CSSMe	-$(CH_2)_5$-
J-37	H	OCF_3	H	H	H	CSSMe	-$(CH_2)_5$-
J-38	H	CF_3	H	H	H	CSSMe	-$(CH_2)_5$-
J-39	H	SMe	H	H	H	CSSMe	-$(CH_2)_5$-
J-40	H	SEt	H	H	H	CSSMe	-$(CH_2)_5$-
J-41	H	SPr^i	H	H	H	CSSMe	-$(CH_2)_5$-
J-42	H	NMe_2	H	H	H	CSSMe	-$(CH_2)_5$-
J-43	H	NEt_2	H	H	H	CSSMe	-$(CH_2)_5$-
J-44	H	H	Cl	H	H	CSSMe	-$(CH_2)_5$-
J-45	H	H	Br	H	H	CSSMe	-$(CH_2)_5$-
J-46	H	H	Me	H	H	CSSMe	-$(CH_2)_5$-
J-47	H	H	Et	H	H	CSSMe	-$(CH_2)_5$-
J-48	H	H	Pr	H	H	CSSMe	-$(CH_2)_5$-
J-49	H	H	Pr^i	H	H	CSSMe	-$(CH_2)_5$-
J-50	H	H	Bu	H	H	CSSMe	-$(CH_2)_5$-

(Table 67)



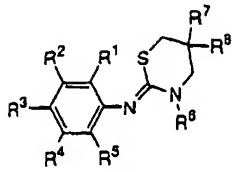
	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
J-51	H	H	Bu^i	H	H	CSSMe	-$(CH_2)_5$-	
J-52	H	H	Bu^s	H	H	CSSMe	-$(CH_2)_5$-	
J-53	H	H	Bu^t	H	H	CSSMe	-$(CH_2)_5$-	
J-54	H	H	OMe	H	H	CSSMe	-$(CH_2)_5$-	
J-55	H	H	OEt	H	H	CSSMe	-$(CH_2)_5$-	
J-56	H	H	OPr	H	H	CSSMe	-$(CH_2)_5$-	
J-57	H	H	OPr^i	H	H	CSSMe	-$(CH_2)_5$-	
J-58	H	H	$OCHF_2$	H	H	CSSMe	-$(CH_2)_5$-	
J-59	H	H	OCF_3	H	H	CSSMe	-$(CH_2)_5$-	
J-60	H	H	CF_3	H	H	CSSMe	-$(CH_2)_5$-	
J-61	H	H	SMe	H	H	CSSMe	-$(CH_2)_5$-	
J-62	H	H	SEt	H	H	CSSMe	-$(CH_2)_5$-	
J-63	H	H	SPr^i	H	H	CSSMe	-$(CH_2)_5$-	
J-64	H	H	NMe_2	H	H	CSSMe	-$(CH_2)_5$-	
J-65	H	H	NEt_2	H	H	CSSMe	-$(CH_2)_5$-	
J-66	Me	NMe_2	H	H	H	CSSMe	-$(CH_2)_5$-	
J-67	NMe_2	Cl	H	H	H	CSSMe	-$(CH_2)_5$-	
J-68	Me	NEt_2	H	H	H	CSSMe	-$(CH_2)_5$-	
J-69	H	NEt_2	Me	H	H	CSSMe	-$(CH_2)_5$-	
J-70	Bu^s	H	H	H	H	CSSMe	-$(CH_2)_5$-	
J-71	OMe	H	OMe	H	H	CSSMe	-$(CH_2)_5$-	
J-72	H	OMe	OMe	H	H	CSSMe	-$(CH_2)_5$-	
J-73	H	OMe	OEt	H	H	CSSMe	-$(CH_2)_5$-	
J-74	H	OEt	OMe	H	H	CSSMe	-$(CH_2)_5$-	
J-75	H	OEt	OEt	H	H	CSSMe	-$(CH_2)_5$-	

(Table 68)



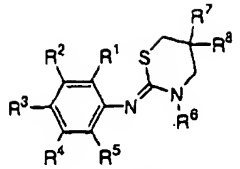
	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
K-1	H	H	H	H	H	COSEt	Et	Et
K-2	Cl	H	H	H	H	COSEt	Et	Et
K-3	Br	H	H	H	H	COSEt	Et	Et
K-4	Me	H	H	H	H	COSEt	Et	Et
K-5	Et	H	H	H	H	COSEt	Et	Et
K-6	Pr	H	H	H	H	COSEt	Et	Et
K-7	Bu	H	H	H	H	COSEt	Et	Et
K-8	Bu^i	H	H	H	H	COSEt	Et	Et
K-9	Bu^t	H	H	H	H	COSEt	Et	Et
K-10	OMe	H	H	H	H	COSEt	Et	Et
K-11	OEt	H	H	H	H	COSEt	Et	Et
K-12	OPr^i	H	H	H	H	COSEt	Et	Et
K-13	OPr	H	H	H	H	COSEt	Et	Et
K-14	$OCHF_2$	H	H	H	H	COSEt	Et	Et
K-15	OCF_3	H	H	H	H	COSEt	Et	Et
K-16	CF_3	H	H	H	H	COSEt	Et	Et
K-17	SMe	H	H	H	H	COSEt	Et	Et
K-18	SEt	H	H	H	H	COSEt	Et	Et
K-19	SPr^i	H	H	H	H	COSEt	Et	Et
K-20	NMe_2	H	H	H	H	COSEt	Et	Et
K-21	NEt_2	H	H	H	H	COSEt	Et	Et
K-22	H	Cl	H	H	H	COSEt	Et	Et
K-23	H	Br	H	H	H	COSEt	Et	Et
K-24	H	Me	H	H	H	COSEt	Et	Et
K-25	H	Et	H	H	H	COSEt	Et	Et

(Table 69)



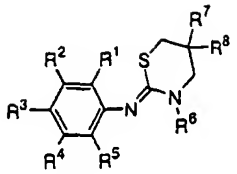
	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
K-26	H	Pr	H	H	H	COSEt	Et	Et
K-27	H	Pr^i	H	H	H	COSEt	Et	Et
K-28	H	Bu	H	H	H	COSEt	Et	Et
K-29	H	Bu^i	H	H	H	COSEt	Et	Et
K-30	H	Bu^s	H	H	H	COSEt	Et	Et
K-31	H	Bu^t	H	H	H	COSEt	Et	Et
K-32	H	OMe	H	H	H	COSEt	Et	Et
K-33	H	OEt	H	H	H	COSEt	Et	Et
K-34	H	OPr	H	H	H	COSEt	Et	Et
K-35	H	OPr^i	H	H	H	COSEt	Et	Et
K-36	H	$OCHF_2$	H	H	H	COSEt	Et	Et
K-37	H	OCF_3	H	H	H	COSEt	Et	Et
K-38	H	CF_3	H	H	H	COSEt	Et	Et
K-39	H	SMe	H	H	H	COSEt	Et	Et
K-40	H	SEt	H	H	H	COSEt	Et	Et
K-41	H	SPr^i	H	H	H	COSEt	Et	Et
K-42	H	NMe_2	H	H	H	COSEt	Et	Et
K-43	H	NEt_2	H	H	H	COSEt	Et	Et
K-44	H	H	Cl	H	H	COSEt	Et	Et
K-45	H	H	Br	H	H	COSEt	Et	Et
K-46	H	H	Me	H	H	COSEt	Et	Et
K-47	H	H	Et	H	H	COSEt	Et	Et
K-48	H	H	Pr	H	H	COSEt	Et	Et
K-49	H	H	Pr^i	H	H	COSEt	Et	Et
K-50	H	H	Bu	H	H	COSEt	Et	Et

(Table 70)



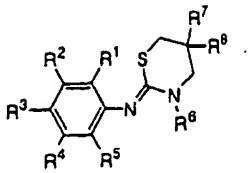
	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
K-51	H	H	Bu^i	H	H	COSEt	Et	Et
K-52	H	H	Bu^s	H	H	COSEt	Et	Et
K-53	H	H	Bu^t	H	H	COSEt	Et	Et
K-54	H	H	OMe	H	H	COSEt	Et	Et
K-55	H	H	OEt	H	H	COSEt	Et	Et
K-56	H	H	OPr	H	H	COSEt	Et	Et
K-57	H	H	OPr^i	H	H	COSEt	Et	Et
K-58	H	H	$OCHF_2$	H	H	COSEt	Et	Et
K-59	H	H	OCF_3	H	H	COSEt	Et	Et
K-60	H	H	CF_3	H	H	COSEt	Et	Et
K-61	H	H	SMe	H	H	COSEt	Et	Et
K-62	H	H	SEt	H	H	COSEt	Et	Et
K-63	H	H	SPr^i	H	H	COSEt	Et	Et
K-64	H	H	NMe_2	H	H	COSEt	Et	Et
K-65	H	H	NEt_2	H	H	COSEt	Et	Et
K-66	Me	NMe_2	H	H	H	COSEt	Et	Et
K-67	NMe_2	Cl	H	H	H	COSEt	Et	Et
K-68	Me	NEt_2	H	H	H	COSEt	Et	Et
K-69	H	NEt_2	Me	H	H	COSEt	Et	Et
K-70	Bu^s	H	H	H	H	COSEt	Et	Et
K-71	OMe	H	OMe	H	H	COSEt	Et	Et
K-72	H	OMe	OMe	H	H	COSEt	Et	Et
K-73	H	OMe	OEt	H	H	COSEt	Et	Et
K-74	H	OEt	OMe	H	H	COSEt	Et	Et
K-75	H	OEt	OEt	H	H	COSEt	Et	Et

(Table 71)



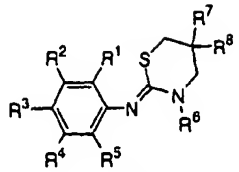
	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
L-1	H	H	H	H	H	COSMe	Et	Et
L-2	Cl	H	H	H	H	COSMe	Et	Et
L-3	Br	H	H	H	H	COSMe	Et	Et
L-4	Me	H	H	H	H	COSMe	Et	Et
L-5	Et	H	H	H	H	COSMe	Et	Et
L-6	Pr	H	H	H	H	COSMe	Et	Et
L-7	Bu	H	H	H	H	COSMe	Et	Et
L-8	Bu^i	H	H	H	H	COSMe	Et	Et
L-9	Bu^t	H	H	H	H	COSMe	Et	Et
L-10	OMe	H	H	H	H	COSMe	Et	Et
L-11	OEt	H	H	H	H	COSMe	Et	Et
L-12	OPr^i	H	H	H	H	COSMe	Et	Et
L-13	OPr	H	H	H	H	COSMe	Et	Et
L-14	$OCHF_2$	H	H	H	H	COSMe	Et	Et
L-15	OCF_3	H	H	H	H	COSMe	Et	Et
L-16	CF_3	H	H	H	H	COSMe	Et	Et
L-17	SMe	H	H	H	H	COSMe	Et	Et
L-18	SEt	H	H	H	H	COSMe	Et	Et
L-19	SPr^i	H	H	H	H	COSMe	Et	Et
L-20	NMe_2	H	H	H	H	COSMe	Et	Et
L-21	NEt_2	H	H	H	H	COSMe	Et	Et
L-22	H	Cl	H	H	H	COSMe	Et	Et
L-23	H	Br	H	H	H	COSMe	Et	Et
L-24	H	Me	H	H	H	COSMe	Et	Et
L-25	H	Et	H	H	H	COSMe	Et	Et

(Table 72)



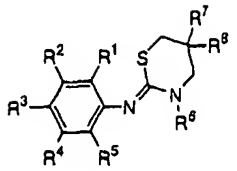
	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
L-26	H	Pr	H	H	H	COSMe	Et	Et
L-27	H	Pr^i	H	H	H	COSMe	Et	Et
L-28	H	Bu	H	H	H	COSMe	Et	Et
L-29	H	Bu^i	H	H	H	COSMe	Et	Et
L-30	H	Bu^s	H	H	H	COSMe	Et	Et
L-31	H	Bu^t	H	H	H	COSMe	Et	Et
L-32	H	OMe	H	H	H	COSMe	Et	Et
L-33	H	OEt	H	H	H	COSMe	Et	Et
L-34	H	OPr	H	H	H	COSMe	Et	Et
L-35	H	OPr^i	H	H	H	COSMe	Et	Et
L-36	H	$OCHF_2$	H	H	H	COSMe	Et	Et
L-37	H	OCF_3	H	H	H	COSMe	Et	Et
L-38	H	CF_3	H	H	H	COSMe	Et	Et
L-39	H	SMe	H	H	H	COSMe	Et	Et
L-40	H	SEt	H	H	H	COSMe	Et	Et
L-41	H	SPr^i	H	H	H	COSMe	Et	Et
L-42	H	NMe_2	H	H	H	COSMe	Et	Et
L-43	H	NEt_2	H	H	H	COSMe	Et	Et
L-44	H	H	Cl	H	H	COSMe	Et	Et
L-45	H	H	Br	H	H	COSMe	Et	Et
L-46	H	H	Me	H	H	COSMe	Et	Et
L-47	H	H	Et	H	H	COSMe	Et	Et
L-48	H	H	Pr	H	H	COSMe	Et	Et
L-49	H	H	Pr^i	H	H	COSMe	Et	Et
L-50	H	H	Bu	H	H	COSMe	Et	Et

(Table 73)



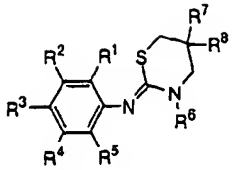
	R^1	R^2	R^3	R^4	R^5	R^6	R^7	R^8
L-51	H	H	Bu^i	H	H	COSMe	Et	Et
L-52	H	H	Bu^s	H	H	COSMe	Et	Et
L-53	H	H	Bu^t	H	H	COSMe	Et	Et
L-54	H	H	OMe	H	H	COSMe	Et	Et
L-55	H	H	OEt	H	H	COSMe	Et	Et
L-56	H	H	OPr	H	H	COSMe	Et	Et
L-57	H	H	OPr^i	H	H	COSMe	Et	Et
L-58	H	H	$OCHF_2$	H	H	COSMe	Et	Et
L-59	H	H	OCF_3	H	H	COSMe	Et	Et
L-60	H	H	CF_3	H	H	COSMe	Et	Et
L-61	H	H	SMe	H	H	COSMe	Et	Et
L-62	H	H	SEt	H	H	COSMe	Et	Et
L-63	H	H	SPr^i	H	H	COSMe	Et	Et
L-64	H	H	NMe_2	H	H	COSMe	Et	Et
L-65	H	H	NEt_2	H	H	COSMe	Et	Et
L-66	Me	NMe_2	H	H	H	COSMe	Et	Et
L-67	NMe_2	Cl	H	H	H	COSMe	Et	Et
L-68	Me	NEt_2	H	H	H	COSMe	Et	Et
L-69	H	NEt_2	Me	H	H	COSMe	Et	Et
L-70	Bu^s	H	H	H	H	COSMe	Et	Et
L-71	Pr^i	H	H	H	H	COSMe	Et	Et
L-72	H	OMe	OMe	H	H	COSMe	Et	Et
L-73	H	OMe	OEt	H	H	COSMe	Et	Et
L-74	H	OEt	OMe	H	H	COSMe	Et	Et
L-75	H	OEt	OEt	H	H	COSMe	Et	Et

(Table 74)



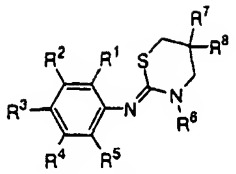
	R^1	R^2	R^3	R^4	R^5	R^6	R^7 R^8
M-1	H	H	H	H	H	COSMe	-$(CH_2)_4$-
M-2	Cl	H	H	H	H	COSMe	-$(CH_2)_4$-
M-3	Br	H	H	H	H	COSMe	-$(CH_2)_4$-
M-4	Me	H	H	H	H	COSMe	-$(CH_2)_4$-
M-5	Et	H	H	H	H	COSMe	-$(CH_2)_4$-
M-6	Pr	H	H	H	H	COSMe	-$(CH_2)_4$-
M-7	Bu	H	H	H	H	COSMe	-$(CH_2)_4$-
M-8	Bu^i	H	H	H	H	COSMe	-$(CH_2)_4$-
M-9	Bu^t	H	H	H	H	COSMe	-$(CH_2)_4$-
M-10	OMe	H	H	H	H	COSMe	-$(CH_2)_4$-
M-11	OEt	H	H	H	H	COSMe	-$(CH_2)_4$-
M-12	OPr^i	H	H	H	H	COSMe	-$(CH_2)_4$-
M-13	OPr	H	H	H	H	COSMe	-$(CH_2)_4$-
M-14	$OCHF_2$	H	H	H	H	COSMe	-$(CH_2)_4$-
M-15	OCF_3	H	H	H	H	COSMe	-$(CH_2)_4$-
M-16	CF_3	H	H	H	H	COSMe	-$(CH_2)_4$-
M-17	SMe	H	H	H	H	COSMe	-$(CH_2)_4$-
M-18	SEt	H	H	H	H	COSMe	-$(CH_2)_4$-
M-19	SPr^i	H	H	H	H	COSMe	-$(CH_2)_4$-
M-20	NMe_2	H	H	H	H	COSMe	-$(CH_2)_4$-
M-21	NEt_2	H	H	H	H	COSMe	-$(CH_2)_4$-
M-22	H	Cl	H	H	H	COSMe	-$(CH_2)_4$-
M-23	H	Br	H	H	H	COSMe	-$(CH_2)_4$-
M-24	H	Me	H	H	H	COSMe	-$(CH_2)_4$-
M-25	H	Et	H	H	H	COSMe	-$(CH_2)_4$-

(Table 75)



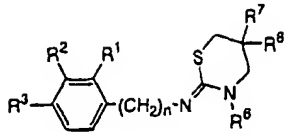
	R^1	R^2	R^3	R^4	R^5	R^6	R^7 R^8
M-26	H	Pr	H	H	H	COSMe	-$(CH_2)_4$-
M-27	H	Pr^i	H	H	H	COSMe	-$(CH_2)_4$-
M-28	H	Bu	H	H	H	COSMe	-$(CH_2)_4$-
M-29	H	Bu^i	H	H	H	COSMe	-$(CH_2)_4$-
M-30	H	Bu^s	H	H	H	COSMe	-$(CH_2)_4$-
M-31	H	Bu^t	H	H	H	COSMe	-$(CH_2)_4$-
M-32	H	OMe	H	H	H	COSMe	-$(CH_2)_4$-
M-33	H	OEt	H	H	H	COSMe	-$(CH_2)_4$-
M-34	H	OPr	H	H	H	COSMe	-$(CH_2)_4$-
M-35	H	OPr^i	H	H	H	COSMe	-$(CH_2)_4$-
M-36	H	$OCHF_2$	H	H	H	COSMe	-$(CH_2)_4$-
M-37	H	OCF_3	H	H	H	COSMe	-$(CH_2)_4$-
M-38	H	CF_3	H	H	H	COSMe	-$(CH_2)_4$-
M-39	H	SMe	H	H	H	COSMe	-$(CH_2)_4$-
M-40	H	SEt	H	H	H	COSMe	-$(CH_2)_4$-
M-41	H	SPr^i	H	H	H	COSMe	-$(CH_2)_4$-
M-42	H	NMe_2	H	H	H	COSMe	-$(CH_2)_4$-
M-43	H	NEt_2	H	H	H	COSMe	-$(CH_2)_4$-
M-44	H	H	Cl	H	H	COSMe	-$(CH_2)_4$-
M-45	H	H	Br	H	H	COSMe	-$(CH_2)_4$-
M-46	H	H	Me	H	H	COSMe	-$(CH_2)_4$-
M-47	H	H	Et	H	H	COSMe	-$(CH_2)_4$-
M-48	H	H	Pr	H	H	COSMe	-$(CH_2)_4$-
M-49	H	H	Pr^i	H	H	COSMe	-$(CH_2)_4$-
M-50	H	H	Bu	H	H	COSMe	-$(CH_2)_4$-

(Table 76)



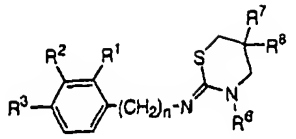
	R^1	R^2	R^3	R^4	R^5	R^6	R^7 R^8
M-51	H	H	Bu^i	H	H	COSMe	$-(CH_2)_4-$
M-52	H	H	Bu^s	H	H	COSMe	$-(CH_2)_4-$
M-53	H	H	Bu^t	H	H	COSMe	$-(CH_2)_4-$
M-54	H	H	OMe	H	H	COSMe	$-(CH_2)_4-$
M-55	H	H	OEt	H	H	COSMe	$-(CH_2)_4-$
M-56	H	H	OPr	H	H	COSMe	$-(CH_2)_4-$
M-57	H	H	OPr^i	H	H	COSMe	$-(CH_2)_4-$
M-58	H	H	$OCHF_2$	H	H	COSMe	$-(CH_2)_4-$
M-59	H	H	OCF_3	H	H	COSMe	$-(CH_2)_4-$
M-60	H	H	CF_3	H	H	COSMe	$-(CH_2)_4-$
M-61	H	H	SMe	H	H	COSMe	$-(CH_2)_4-$
M-62	H	H	SEt	H	H	COSMe	$-(CH_2)_4-$
M-63	H	H	SPr^i	H	H	COSMe	$-(CH_2)_4-$
M-64	H	H	NMe_2	H	H	COSMe	$-(CH_2)_4-$
M-65	H	H	NEt_2	H	H	COSMe	$-(CH_2)_4-$
M-66	Me	NMe_2	H	H	H	COSMe	$-(CH_2)_4-$
M-67	NMe_2	Cl	H	H	H	COSMe	$-(CH_2)_4-$
M-68	Me	NEt_2	H	H	H	COSMe	$-(CH_2)_4-$
M-69	H	NEt_2	Me	H	H	COSMe	$-(CH_2)_4-$
M-70	Bu^s	H	H	H	H	COSMe	$-(CH_2)_4-$
M-71	Pr^i	H	H	H	H	COSMe	$-(CH_2)_4-$
M-72	H	OMe	OMe	H	H	COSMe	$-(CH_2)_4-$
M-73	H	OMe	OEt	H	H	COSMe	$-(CH_2)_4-$
M-74	H	OEt	OMe	H	H	COSMe	$-(CH_2)_4-$
M-75	H	OEt	OEt	H	H	COSMe	$-(CH_2)_4-$

(Table 77)



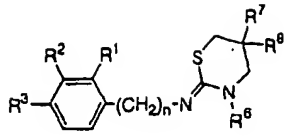
	R^1	R^2	R^3	n	R^6	R^7	R^8
R-1	H	H	H	1	CSSMe	Me	Me
R-2	Cl	H	H	1	CSSMe	Me	Me
R-3	Br	H	H	1	CSSMe	Me	Me
R-4	Me	H	H	1	CSSMe	Me	Me
R-5	Et	H	H	1	CSSMe	Me	Me
R-6	Pr	H	H	1	CSSMe	Me	Me
R-7	Bu	H	H	1	CSSMe	Me	Me
R-8	Bu^i	H	H	1	CSSMe	Me	Me
R-9	Bu^t	H	H	1	CSSMe	Me	Me
R-10	Pr^i	H	H	1	CSSMe	Me	Me
R-11	OEt	H	H	1	CSSMe	Me	Me
R-12	OPr^i	H	H	1	CSSMe	Me	Me
R-13	OPr	H	H	1	CSSMe	Me	Me
R-14	$OCHF_2$	H	H	1	CSSMe	Me	Me
R-15	OCF_3	H	H	1	CSSMe	Me	Me
R-16	CF_3	H	H	1	CSSMe	Me	Me
R-17	SMe	H	H	1	CSSMe	Me	Me
R-18	SEt	H	H	1	CSSMe	Me	Me
R-19	SPr^i	H	H	1	CSSMe	Me	Me
R-20	NMe_2	H	H	1	CSSMe	Me	Me
R-21	NEt_2	H	H	1	CSSMe	Me	Me
R-22	H	Cl	H	1	CSSMe	Me	Me
R-23	H	Br	H	1	CSSMe	Me	Me
R-24	H	Me	H	1	CSSMe	Me	Me
R-25	H	Et	H	1	CSSMe	Me	Me

(Table 78)



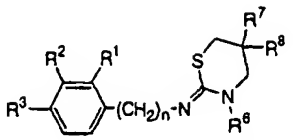
	R^1	R^2	R^3	n	R^6	R^7	R^8
R-26	H	Pr	H	1	CSSMe	Me	Me
R-27	H	Pr^i	H	1	CSSMe	Me	Me
R-28	H	Bu	H	1	CSSMe	Me	Me
R-29	H	Bu^i	H	1	CSSMe	Me	Me
R-30	H	Bu^s	H	1	CSSMe	Me	Me
R-31	H	Bu^t	H	1	CSSMe	Me	Me
R-32	H	OMe	H	1	CSSMe	Me	Me
R-33	H	OEt	H	1	CSSMe	Me	Me
R-34	H	OPr	H	1	CSSMe	Me	Me
R-35	H	OPr^i	H	1	CSSMe	Me	Me
R-36	H	$OCHF_2$	H	1	CSSMe	Me	Me
R-37	H	OCF_3	H	1	CSSMe	Me	Me
R-38	H	CF_3	H	1	CSSMe	Me	Me
R-39	H	SMe	H	1	CSSMe	Me	Me
R-40	H	SEt	H	1	CSSMe	Me	Me
R-41	H	SPr^i	H	1	CSSMe	Me	Me
R-42	H	NMe_2	H	1	CSSMe	Me	Me
R-43	H	NEt_2	H	1	CSSMe	Me	Me
R-44	Cl	H	Cl	1	CSSMe	Me	Me
R-45	H	H	Br	1	CSSMe	Me	Me
R-46	H	H	Me	1	CSSMe	Me	Me
R-47	H	H	Et	1	CSSMe	Me	Me
R-48	H	H	Pr	1	CSSMe	Me	Me
R-49	H	H	Pr^i	1	CSSMe	Me	Me
R-50	H	H	Bu	1	CSSMe	Me	Me

(Table 79)



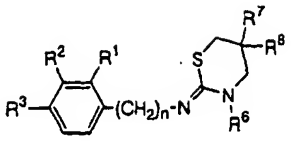
	R^1	R^2	R^3	n	R^6	R^7	R^8
R-51	H	H	Bu^i	1	CSSMe	Me	Me
R-52	H	H	Bu^s	1	CSSMe	Me	Me
R-53	H	H	Bu^t	1	CSSMe	Me	Me
R-54	H	H	OMe	1	CSSMe	Me	Me
R-55	H	H	OEt	1	CSSMe	Me	Me
R-56	H	H	OPr	1	CSSMe	Me	Me
R-57	H	H	OPr^i	1	CSSMe	Me	Me
R-58	H	H	$OCHF_2$	1	CSSMe	Me	Me
R-59	H	H	OCF_3	1	CSSMe	Me	Me
R-60	H	H	CF_3	1	CSSMe	Me	Me
R-61	H	H	SMe	1	CSSMe	Me	Me
R-62	H	H	SEt	1	CSSMe	Me	Me
R-63	H	H	SPr^i	1	CSSMe	Me	Me
R-64	H	H	NMe_2	1	CSSMe	Me	Me
R-65	H	H	NEt_2	1	CSSMe	Me	Me
R-66	Me	NMe_2	H	1	CSSMe	Me	Me
R-67	NMe_2	Cl	H	1	CSSMe	Me	Me
R-68	Me	NEt_2	H	1	CSSMe	Me	Me
R-69	H	NEt_2	Me	1	CSSMe	Me	Me
R-70	Bu^s	H	H	1	CSSMe	Me	Me
R-71	OMe	H	OMe	1	CSSMe	Me	Me
R-72	H	OMe	OMe	1	CSSMe	Me	Me
R-73	H	OMe	OEt	1	CSSMe	Me	Me
R-74	H	OEt	OMe	1	CSSMe	Me	Me
R-75	H	OEt	OEt	1	CSSMe	Me	Me

(Table 80)



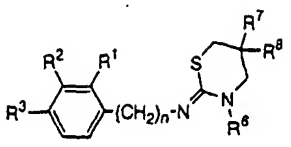
	R^1	R^2	R^3	n	R^6	R^7	R^8
O-1	H	H	H	2	CSSMe	Me	Me
O-2	Cl	H	H	2	CSSMe	Me	Me
O-3	Br	H	H	2	CSSMe	Me	Me
O-4	Me	H	H	2	CSSMe	Me	Me
O-5	Et	H	H	2	CSSMe	Me	Me
O-6	Pr	H	H	2	CSSMe	Me	Me
O-7	Bu	H	H	2	CSSMe	Me	Me
O-8	Bu^i	H	H	2	CSSMe	Me	Me
O-9	Bu^t	H	H	2	CSSMe	Me	Me
O-10	Pr^i	H	H	2	CSSMe	Me	Me
O-11	OEt	H	H	2	CSSMe	Me	Me
O-12	OPr^i	H	H	2	CSSMe	Me	Me
O-13	OPr	H	H	2	CSSMe	Me	Me
O-14	$OCHF_2$	H	H	2	CSSMe	Me	Me
O-15	OCF_3	H	H	2	CSSMe	Me	Me
O-16	CF_3	H	H	2	CSSMe	Me	Me
O-17	SMe	H	H	2	CSSMe	Me	Me
O-18	SEt	H	H	2	CSSMe	Me	Me
O-19	SPr^i	H	H	2	CSSMe	Me	Me
O-20	NMe_2	H	H	2	CSSMe	Me	Me
O-21	NEt_2	H	H	2	CSSMe	Me	Me
O-22	H	Cl	H	2	CSSMe	Me	Me
O-23	H	Br	H	2	CSSMe	Me	Me
O-24	H	Me	H	2	CSSMe	Me	Me
O-25	H	Et	H	2	CSSMe	Me	Me

(Table 81)



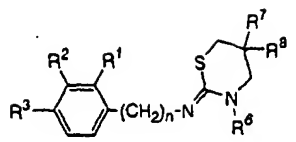
	R^1	R^2	R^3	m	R^6	R^7	R^8
O-26	H	Pr	H	2	CSSMe	Me	Me
O-27	H	Pr^i	H	2	CSSMe	Me	Me
O-28	H	Bu	H	2	CSSMe	Me	Me
O-29	H	Bu^i	H	2	CSSMe	Me	Me
O-30	H	Bu^s	H	2	CSSMe	Me	Me
O-31	H	Bu^t	H	2	CSSMe	Me	Me
O-32	H	OMe	H	2	CSSMe	Me	Me
O-33	H	OEt	H	2	CSSMe	Me	Me
O-34	H	OPr	H	2	CSSMe	Me	Me
O-35	H	OPr^i	H	2	CSSMe	Me	Me
O-36	H	$OCHF_2$	H	2	CSSMe	Me	Me
O-37	H	OCF_3	H	2	CSSMe	Me	Me
O-38	H	CF_3	H	2	CSSMe	Me	Me
O-39	H	SMe	H	2	CSSMe	Me	Me
O-40	H	SEt	H	2	CSSMe	Me	Me
O-41	H	SPr^i	H	2	CSSMe	Me	Me
O-42	H	NMe_2	H	2	CSSMe	Me	Me
O-43	H	NEt_2	H	2	CSSMe	Me	Me
O-44	F	H	F	2	CSSMe	Me	Me
O-45	H	H	Br	2	CSSMe	Me	Me
O-46	H	H	Me	2	CSSMe	Me	Me
O-47	H	H	Et	2	CSSMe	Me	Me
O-48	H	H	Pr	2	CSSMe	Me	Me
O-49	H	H	Pr^i	2	CSSMe	Me	Me
O-50	H	H	Bu	2	CSSMe	Me	Me

(Table 82)



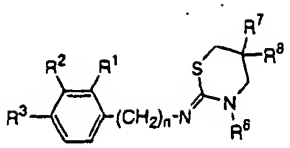
	R^1	R^2	R^3	n	R^6	R^7	R^8
O-51	H	H	Bu^i	2	CSSMe	Me	Me
O-52	H	H	Bu^s	2	CSSMe	Me	Me
O-53	H	H	Bu^t	2	CSSMe	Me	Me
O-54	H	H	OMe	2	CSSMe	Me	Me
O-55	H	H	OEt	2	CSSMe	Me	Me
O-56	H	H	OPr	2	CSSMe	Me	Me
O-57	H	H	OPr^i	2	CSSMe	Me	Me
O-58	H	H	$OCHF_2$	2	CSSMe	Me	Me
O-59	H	H	OCF_3	2	CSSMe	Me	Me
O-60	H	H	CF_3	2	CSSMe	Me	Me
O-61	H	H	SMe	2	CSSMe	Me	Me
O-62	H	H	SEt	2	CSSMe	Me	Me
O-63	H	H	SPr^i	2	CSSMe	Me	Me
O-64	H	H	NMe_2	2	CSSMe	Me	Me
O-65	H	H	NEt_2	2	CSSMe	Me	Me
O-66	Me	NMe_2	H	2	CSSMe	Me	Me
O-67	NMe_2	Cl	H	2	CSSMe	Me	Me
O-68	Me	NEt_2	H	2	CSSMe	Me	Me
O-69	H	NEt_2	Me	2	CSSMe	Me	Me
O-70	Bu^s	H	H	2	CSSMe	Me	Me
O-71	OMe	H	OMe	2	CSSMe	Me	Me
O-72	H	OMe	OMe	2	CSSMe	Me	Me
O-73	H	OMe	OEt	2	CSSMe	Me	Me
O-74	H	OEt	OMe	2	CSSMe	Me	Me
O-75	H	OEt	OEt	2	CSSMe	Me	Me

(Table 83)



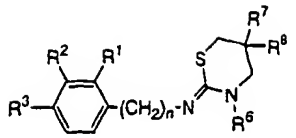
	R^1	R^2	R^3	n	R^6	R^7	R^8
P-1	H	H	H	1	CSSMe	Et	Et
P-2	Cl	H	H	1	CSSMe	Et	Et
P-3	Br	H	H	1	CSSMe	Et	Et
P-4	Me	H	H	1	CSSMe	Et	Et
P-5	Et	H	H	1	CSSMe	Et	Et
P-6	Pr	H	H	1	CSSMe	Et	Et
P-7	Bu	H	H	1	CSSMe	Et	Et
P-8	Bu^i	H	H	1	CSSMe	Et	Et
P-9	Bu^t	H	H	1	CSSMe	Et	Et
P-10	Pr^i	H	H	1	CSSMe	Et	Et
P-11	OEt	H	H	1	CSSMe	Et	Et
P-12	OPr^i	H	H	1	CSSMe	Et	Et
P-13	OPr	H	H	1	CSSMe	Et	Et
P-14	$OCHF_2$	H	H	1	CSSMe	Et	Et
P-15	OCF_3	H	H	1	CSSMe	Et	Et
P-16	CF_3	H	H	1	CSSMe	Et	Et
P-17	SMe	H	H	1	CSSMe	Et	Et
P-18	SEt	H	H	1	CSSMe	Et	Et
P-19	SPr^i	H	H	1	CSSMe	Et	Et
P-20	NMe_2	H	H	1	CSSMe	Et	Et
P-21	NEt_2	H	H	1	CSSMe	Et	Et
P-22	H	Cl	H	1	CSSMe	Et	Et
P-23	H	Br	H	1	CSSMe	Et	Et
P-24	H	Me	H	1	CSSMe	Et	Et
P-25	H	Et	H	1	CSSMe	Et	Et

(Table 84)



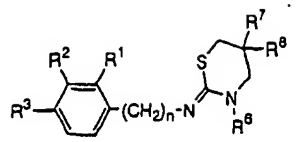
	R¹	R²	R³	n	R⁶	R⁷	R⁸
P-26	H	Pr	H	1	CSSMe	Et	Et
P-27	H	Pr^i	H	1	CSSMe	Et	Et
P-28	H	Bu	H	1	CSSMe	Et	Et
P-29	H	Bu^i	H	1	CSSMe	Et	Et
P-30	H	Bu^s	H	1	CSSMe	Et	Et
P-31	H	Bu^t	H	1	CSSMe	Et	Et
P-32	H	OMe	H	1	CSSMe	Et	Et
P-33	H	OEt	H	1	CSSMe	Et	Et
P-34	H	OPr	H	1	CSSMe	Et	Et
P-35	H	OPr^i	H	1	CSSMe	Et	Et
P-36	H	$OCHF_2$	H	1	CSSMe	Et	Et
P-37	H	OCF_3	H	1	CSSMe	Et	Et
P-38	H	CF_3	H	1	CSSMe	Et	Et
P-39	H	SMe	H	1	CSSMe	Et	Et
P-40	H	SEt	H	1	CSSMe	Et	Et
P-41	H	SPr^i	H	1	CSSMe	Et	Et
P-42	H	NMe_2	H	1	CSSMe	Et	Et
P-43	H	NEt_2	H	1	CSSMe	Et	Et
P-44	OMe	H	H	1	CSSMe	Et	Et
P-45	H	H	Br	1	CSSMe	Et	Et
P-46	H	H	Me	1	CSSMe	Et	Et
P-47	H	H	Et	1	CSSMe	Et	Et
P-48	H	H	Pr	1	CSSMe	Et	Et
P-49	H	H	Pr^i	1	CSSMe	Et	Et
P-50	H	H	Bu	1	CSSMe	Et	Et

(Table 85)



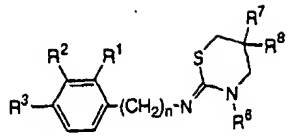
	R^1	R^2	R^3	n	R^6	R^7	R^8
P-51	H	H	Bu^i	1	CSSMe	Et	Et
P-52	H	H	Bu^s	1	CSSMe	Et	Et
P-53	H	H	Bu^t	1	CSSMe	Et	Et
P-54	H	H	OMe	1	CSSMe	Et	Et
P-55	H	H	OEt	1	CSSMe	Et	Et
P-56	H	H	OPr	1	CSSMe	Et	Et
P-57	H	H	OPr^i	1	CSSMe	Et	Et
P-58	H	H	$OCHF_2$	1	CSSMe	Et	Et
P-59	H	H	OCF_3	1	CSSMe	Et	Et
P-60	H	H	CF_3	1	CSSMe	Et	Et
P-61	H	H	SMe	1	CSSMe	Et	Et
P-62	H	H	SEt	1	CSSMe	Et	Et
P-63	H	H	SPr^i	1	CSSMe	Et	Et
P-64	H	H	NMe_2	1	CSSMe	Et	Et
P-65	H	H	NEt_2	1	CSSMe	Et	Et
P-66	Me	NMe_2	H	1	CSSMe	Et	Et
P-67	NMe_2	Cl	H	1	CSSMe	Et	Et
P-68	Me	NEt_2	H	1	CSSMe	Et	Et
P-69	H	NEt_2	Me	1	CSSMe	Et	Et
P-70	Bu^s	H	H	1	CSSMe	Et	Et
P-71	OMe	H	OMe	1	CSSMe	Et	Et
P-72	H	OMe	OMe	1	CSSMe	Et	Et
P-73	H	OMe	OEt	1	CSSMe	Et	Et
P-74	H	OEt	OMe	1	CSSMe	Et	Et
P-75	H	OEt	OEt	1	CSSMe	Et	Et

(Table 86)



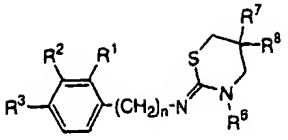
	R^1	R^2	R^3	n	R^6	R^7	R^8
Q-1	H	H	H	2	CSSMe	Et	Et
Q-2	Cl	H	H	2	CSSMe	Et	Et
Q-3	Br	H	H	2	CSSMe	Et	Et
Q-4	Me	H	H	2	CSSMe	Et	Et
Q-5	Et	H	H	2	CSSMe	Et	Et
Q-6	Pr	H	H	2	CSSMe	Et	Et
Q-7	Bu	H	H	2	CSSMe	Et	Et
Q-8	Bu^i	H	H	2	CSSMe	Et	Et
Q-9	Bu^t	H	H	2	CSSMe	Et	Et
Q-10	Pr^i	H	H	2	CSSMe	Et	Et
Q-11	OEt	H	H	2	CSSMe	Et	Et
Q-12	OPr^i	H	H	2	CSSMe	Et	Et
Q-13	OPr	H	H	2	CSSMe	Et	Et
Q-14	$OCHF_2$	H	H	2	CSSMe	Et	Et
Q-15	OCF_3	H	H	2	CSSMe	Et	Et
Q-16	CF_3	H	H	2	CSSMe	Et	Et
Q-17	SMe	H	H	2	CSSMe	Et	Et
Q-18	SEt	H	H	2	CSSMe	Et	Et
Q-19	SPr^i	H	H	2	CSSMe	Et	Et
Q-20	NMe_2	H	H	2	CSSMe	Et	Et
Q-21	NEt_2	H	H	2	CSSMe	Et	Et
Q-22	H	Cl	H	2	CSSMe	Et	Et
Q-23	H	Br	H	2	CSSMe	Et	Et
Q-24	H	Me	H	2	CSSMe	Et	Et
Q-25	H	Et	H	2	CSSMe	Et	Et

(Table 87)



	R^1	R^2	R^3	m	R^6	R^7	R^8
Q-26	H	Pr	H	2	CSSMe	Et	Et
Q-27	H	Pr^i	H	2	CSSMe	Et	Et
Q-28	H	Bu	H	2	CSSMe	Et	Et
Q-29	H	Bu^i	H	2	CSSMe	Et	Et
Q-30	H	Bu^s	H	2	CSSMe	Et	Et
Q-31	H	Bu^t	H	2	CSSMe	Et	Et
Q-32	H	OMe	H	2	CSSMe	Et	Et
Q-33	H	OEt	H	2	CSSMe	Et	Et
Q-34	H	OPr	H	2	CSSMe	Et	Et
Q-35	H	OPr^i	H	2	CSSMe	Et	Et
Q-36	H	$OCHF_2$	H	2	CSSMe	Et	Et
Q-37	H	OCF_3	H	2	CSSMe	Et	Et
Q-38	H	CF_3	H	2	CSSMe	Et	Et
Q-39	H	SMe	H	2	CSSMe	Et	Et
Q-40	H	SEt	H	2	CSSMe	Et	Et
Q-41	H	SPr^i	H	2	CSSMe	Et	Et
Q-42	H	NMe_2	H	2	CSSMe	Et	Et
Q-43	H	NEt_2	H	2	CSSMe	Et	Et
Q-44	OMe	H	H	2	CSSMe	Et	Et
Q-45	H	H	Br	2	CSSMe	Et	Et
Q-46	H	H	Me	2	CSSMe	Et	Et
Q-47	H	H	Et	2	CSSMe	Et	Et
Q-48	H	H	Pr	2	CSSMe	Et	Et
Q-49	H	H	Pr^i	2	CSSMe	Et	Et
Q-50	H	H	Bu	2	CSSMe	Et	Et

(Table 88)



	R^1	R^2	R^3	n	R^6	R^7	R^8
Q-51	H	H	Bu^i	2	CSSMe	Et	Et
Q-52	H	H	Bu^s	2	CSSMe	Et	Et
Q-53	H	H	Bu^t	2	CSSMe	Et	Et
Q-54	H	H	OMe	2	CSSMe	Et	Et
Q-55	H	H	OEt	2	CSSMe	Et	Et
Q-56	H	H	OPr	2	CSSMe	Et	Et
Q-57	H	H	OPr^i	2	CSSMe	Et	Et
Q-58	H	H	$OCHF_2$	2	CSSMe	Et	Et
Q-59	H	H	OCF_3	2	CSSMe	Et	Et
Q-60	H	H	CF_3	2	CSSMe	Et	Et
Q-61	H	H	SMe	2	CSSMe	Et	Et
Q-62	H	H	SEt	2	CSSMe	Et	Et
Q-63	H	H	SPr^i	2	CSSMe	Et	Et
Q-64	H	H	NMe_2	2	CSSMe	Et	Et
Q-65	H	H	NEt_2	2	CSSMe	Et	Et
Q-66	Me	NMe_2	H	2	CSSMe	Et	Et
Q-67	NMe_2	Cl	H	2	CSSMe	Et	Et
Q-68	Me	NEt_2	H	2	CSSMe	Et	Et
Q-69	H	NEt_2	Me	2	CSSMe	Et	Et
Q-70	Bu^s	H	H	2	CSSMe	Et	Et
Q-71	OMe	H	OMe	2	CSSMe	Et	Et
Q-72	H	OMe	OMe	2	CSSMe	Et	Et
Q-73	H	OMe	OEt	2	CSSMe	Et	Et
Q-74	H	OEt	OMe	2	CSSMe	Et	Et
Q-75	H	OEt	OEt	2	CSSMe	Et	Et

[0143] The above compounds of the present invention were examined as shown below.

Example 1: Experiments for Human CB2 receptor (CB2R) binding inhibition

[0144] The coding region of human CB2R cDNA (Munro *etc,* Nature, 1993, 365, 61-65) was inserted into the mammalian expression vector, pSVL SV40 Late Promoter Expression Vector (Amersham Pharmacia Biotech Inc.). The prepared vector was transfected into Chinese Hamster Ovary (CHO) cells with LipofectAMINE reagent (Gibco BRL) according to the manufacture's protocol, and the stable CB2R-expressing clones were selected.

[0145] The crude membrane fractions were then prepared from the CB2R-expressing CHO cells. Receptor binding assay was performed by incubating the membranes with each test compound and [^{3}H]CP55940 (at a final concentration of 0.5 nM: NEN Life Science Products) in the assay buffer (50 mM Tris-HCl, 1 mM EDTA, 3 mM $MgCl_2$, pH 7.4) containing 0.5% bovine serum albumin (BSA) for 2 hr at 25 °C. The incubation mixture was filtered through 1% polyethylenimine (PEI)-treated GF/C glass filter and washed with 50 mM Tris-HCl (pH 7.4) containing 0.1% BSA. The radioactivity was then counted with a liquid scintillation counter. Nonspecific binding was determined in the presence of 10 μM WIN55212-2 (a CB agonist described in the patent US508122, Research Biochemicals International), and the specific binding was calculated by subtracting the nonspecific binding from the total binding. The IC_{50} value for each test compound was determined as the concentration at which 50 % of the specific binding was inhibited.

[0146] For the receptor binding assay of human CB1 receptor (CB1R), the stable CB1R-expressing CHO cells were

prepared as described above, and the binding assay was performed with their membrane fractions. As a consequence of these studies, the Ki values of each test compound for both cannabinoid receptors were determined, which were presented in Table 89. As shown in this table, a series of compounds described in the present invention were found to selectively block the binding of CP55940 (a CB agonist described in the patent US 4371720) to CB2R more effectively than CB1R.

(Table 89)

Compound No.		Ki (nM)
	CB1receptor	CB2receptor
I-5	>5000	61
I-23	>5000	29
I-50	>5000	39
I-51	n.t.	23
I-52	n.t.	35
I-56	n.t.	54
I-6	>5000	9
I-57	4134	6
I-69	n.t.	33
I-60	2097	18
I-62	n.t.	44
I-63	n.t.	43
I-74	n.t.	48
I-77	n.t.	53
I-84	>5000	35
I-85	n.t.	25
n.t.: not tested		

Example 2: Inhibition experiments for CB2R-mediated suppression of cAMP synthesis

[0147] The CHO cells expressing human CB2R were incubated with test compounds for 15 min. After the incubation, 4 μM forskolin (Sigma) was added and the cells were incubated for 20 min at 37 °C. The reaction was stopped by the addition of IN HCl and the amount of cAMP in the cell supernatant was measured using an EIA kit (Amersham Pharmacia Biotech) according to the manufacture's protocol. The cAMP amount increased by forskolin compared to that in the absence of forskolin was defined as 100%, and the IC_{50} value of each test compound was determined as the concentration at which 50 % of the forskolin-stimulated cAMP synthesis was inhibited. As a consequence of these studies, the IC_{50} value of each test compound was presented in Table 90. As shown in Table 90, the compounds described in the present invention were found to possess agonistic activity toward CB2R.

[0148] The antagonistic activity of each compound was also evaluated in this assay.

(Table 90)

Compound No.	IC_{50} (nM)
I-5	6.5
I-23	2.6
I-51	2.8
I-6	2.7
I-57	5.5

Example 3: Experiments for Sheep red blood cell (SRBC)-induced delayed type hypersensitive (DTH) reaction

[0149] Female ddY mice (7 weeks old) were used for the sheep red blood cell (SRBC)-induced delayed type hypersensitive (DTH) reaction.

[0150] Cannabinoid receptor agonist, I-6, I-60, I-77 and I-118 were suspended in 0.6% arabic gum solution. Mice were sensitized by the intradermal injection of 10^7 cells of SRBC (40μl/foot) into the left hind foot pad. After 5 days,

DTH reaction was induced by the intradermal injection of 10^8 cells of SRBC in the right hind foot pad. Test compounds were administerd *p.o.* (10 ml/kg) 1 hr before and 5 hr after the induction of DTH reaction. After 24 hrs of the injection of SRBC, the left and right foot pad volumes were measured by the water displacement method. The foot pad swelling was calculated as the differences in the volumes between the right and left hind foot pad, and used as an index of the DTH reaction.

[0151] Data are expressed as the inhibition percentage of each compound. Statistical analysis was performed with Welch's t-test, in which the value of $P<0.05$ is considered as a significant difference.

(Table 91)

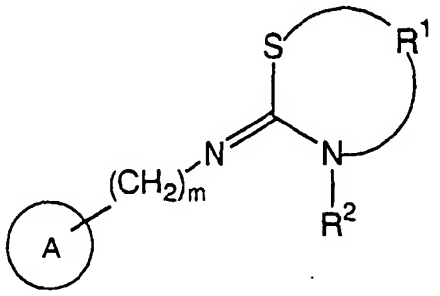
Comp. No.	Dose (mg/kg)	Inhibition percentage (%)
I-6	40	45.2
I-60	30	31.1
I-77	30	33.8
I-118	30	33.0

Industrial Applicability

[0152] The compound of the formula (I) and (II) of the present invention selectively binds to the cannabinoid type 2 receptor (CB2R) to exhibit an antagonistic activity or agonistic activity to CB2R. Therefore, the present compound neither causes side effects on the central nervous system such as illusion or the drug dependence associated with the cannabinoid type 1 receptor (CB1R) and can be used for treating or preventing diseases associated with the cannabinoid type 2 receptor (CB2R).

Claims

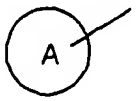
1. A pharmaceutical composition of a compound of the formula (I):



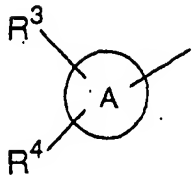
(I)

wherein R^1 is optionally substituted alkylene, R^2 is alkyl; a group of the formula: $-C(=R^5)-R^6$ wherein R^5 is O or S, R^6 is alkyl, alkoxy, alkylthio, optionally substituted amino, optionally substituted aralkyloxy, optionally substituted aralkylthio, optionally substituted aralkylamino, alkoxyalkyl, alkylthioalkyl or optionally substituted aminoalkyl; or a group of the formula: $-SO_2R^7$ wherein R^7 is alkyl, optionally substituted amino, optionally substituted aryl or optionally substituted heteroaryl, m is an integer of 1 to 2, A is optionally substituted aromatic carbocycle or optionally substituted aromatic heterocycle, a prodrug of itself, a pharmaceutically acceptable salt thereof or a solvate thereof.

2. The pharmaceutical composition according to claim 1 wherein the group of the formula:



is a group of the formula:



wherein R^3 and R^4 each is independently, hydrogen, alkyl, alkoxy, alkylthio, optionally substituted amino, optionally substituted aryl, optionally substituted aryloxy, cycloalkyl, halogen, hydroxy, nitro, haloalkyl, haloalkoxy, optionally substituted carbamoyl, carboxy, alkoxycarbonyl, alkylsulfinyl, alkylsulfonyl, alkoxyalkyl, alkylthioalkyl, optionally substituted aminoalkyl, alkoxyalkoxy, alkylthioalkoxy, optionally substituted heteroaryl, optionally substituted non-aromatic heterocyclic group, alkoxyiminoalkyl or a group of the formula: $-C(=O)-R^H$ wherein R^H is hydrogen, alkyl, optionally substituted aryl or optionally substituted non-aromatic heterocyclic group,
or R^3 and R^4 taken together may form alkylenedioxy, A is optionally substituted aromatic carbocycle or optionally substituted aromatic heterocycle.

3. The pharmaceutical composition according to claim 1 or 2 which has a binding activity to a cannabinoid type 2 receptor.

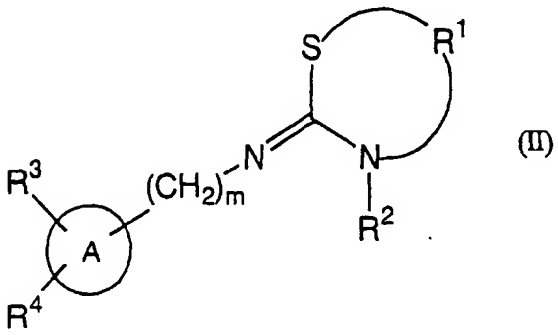
4. The pharmaceutical composition according to claim 3 which has an agonistic activity to a cannabinoid type 2 receptor.

5. The pharmaceutical composition according to claim 3 which is useful as an anti-inflammatory agent.

6. The pharmaceutical composition according to claim 3 which is useful as an immunosuppressive agent.

7. The pharmaceutical composition according to claim 3 which is useful as a nephritis treating agent.

8. A compound of the formula (II):



(II)

wherein R^1 is optionally substituted alkylene, R^2 is a group of the formula: $-C(=R^5)-R^6$ wherein R^5 is O or S, R^6 is alkyl, alkoxy, alkylthio, optionally substituted amino, optionally substituted aralkyloxy, optionally substituted aralkylthio, optionally substituted aralkylamino, alkoxyalkyl, alkylthioalkyl, or optionally substituted aminoalkyl; or a group of the formula: $-SO_2R^7$ wherein R^7 is alkyl, optionally substituted amino, optionally substituted aryl or optionally substituted heteroaryl, R^3 and R^4 each is independently hydrogen, alkyl, alkoxy, alkylthio, optionally substituted amino, optionally substituted aryl, optionally substituted aryloxy, cycloalkyl, halogen, hydroxy, nitro, haloalkyl, haloalkoxy, optionally substituted carbamoyl, carboxy, alkoxycarbonyl, alkylsulfinyl, alkylsulfonyl, alkoxyalkyl, alkylthioalkyl, optionally substituted aminoalkyl, alkoxyalkoxy, alkylthioalkoxy, optionally substituted heteroaryl, optionally substituted non-aromatic heterocyclic group, alkoxyiminoalkyl, or a group of the formula: $-C(=O)-R^H$ wherein R^H is hydrogen, alkyl, optionally substituted aryl or optionally substituted non-aromatic heterocyclic

group, or
R^3 and R^4 taken together may form alkylenedioxy, m is an integer of 0 to 2, A is optionally substituted aromatic carbocycle or optionally substituted aromatic heterocycle, a prodrug of itself, a pharmaceutically acceptable salt thereof or a solvate thereof.

9. The compound according to claim 8 wherein m is 0, a prodrug of itself, a pharmaceutically acceptable salt thereof or a solvate thereof.

10. The compound according to claim 8 or 9 wherein R^1 is a C2-C9 straight or branched alkylene optionally substituted with alkylene, a prodrug of itself, a pharmaceutically acceptable salt thereof or a solvate thereof.

11. The compound according to any one of claims 8 to 10 wherein R^1 is a C2-C9 straight alkylene substituted with alkylene, or a C2-C9 branched alkylene, a prodrug of itself, a pharmaceutically acceptable salt thereof or a solvate thereof.

12. The compound according to any one of claims 8 to 11 wherein R^6 is alkoxy or alkylthio, and R^7 is optionally substituted aryl, a prodrug of itself, a pharmaceutically acceptable salt thereof or a solvate thereof.

13. The compound according to any one of claims 8 to 12 wherein R^3 and R^4 each is independently hydrogen, alkyl, alkoxy or alkylthio, and A is optionally substituted aromatic carbocycle, a prodrug of itself, a pharmaceutically acceptable salt thereof or a solvate thereof.

14. The compound according to claim 8 wherein R^1 is 2,2-dimethyltrimethylene, 2,2-diethyltrimethylene, 2,2-ethylenetrimethylene, 1-methyltrimethylene, 2-methyltrimethylene, trimethylene, 2,2-di-n-propyltrimethylene, 2,2-tetramethylenetrimethylene, 2,2-pentamethylenetrimethylene, 1,1-dimethylethylene or 1-methylethylene, R^6 is methyl, ethyl, n-propyl, i-propyl, methoxy, ethoxy, n-propoxy, i-propoxy, n-butoxy, methylthio, ethylthio, n-propylthio, i-propylthio, i-butylthio, sec-butylthio, benzyloxy, benzylthio, methoxymethyl, ethoxymethyl, methylthiomethyl, ethylthiomethyl or ethylamino, R^7 is methyl, ethyl, 4-tolyl, 4-nitrophenyl, 3-nitrophenyl, 2-nitrophenyl, 4-methoxyphenyl, 4-trifluoromethylphenyl, 2-thienyl or 2-naphthyl, R^3 is hydrogen, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, sec-butyl, t-butyl, methoxy, ethoxy, n-propoxy, i-propoxy, n-butoxy, methylthio, ethylthio, n-propylthio, i-propylthio, dimethylamino, acetylamino, N-acetylmethylamino, diethylamino, ethylmethylamino, propylmethylamino, phenyl, phenoxy, fluoro, chloro, bromo, nitro, trifluoromethyl, difluoromethoxy, trifluoromethoxy, N-methylcarbamoyl, methoxycarbonyl, methanesulfinyl, ethanesulfinyl, methanesulfonyl, ethanesulfonyl, acetyl, methoxymethyl, 1-methoxyethyl, 3-pyridyl, morpholino, pyrrolidino, piperidino, 2-oxopyrrolidino, 1-methoxyiminoethyl or morpholinocarbonyl, R^4 is hydrogen, methyl, ethyl, fluoro, chloro, nitro, methoxy or ethoxy, or
R^3 and R^4 taken together may form $-O-CH_2-O-$, A is benzene, naphthalene, pyridine or quinoline, a prodrug of itself, a pharmaceutically acceptable salt thereof or a solvate thereof.

15. A pharmaceutical composition which comprises the compound according to any one of claims 8 to 14, a prodrug of itself, a pharmaceutically acceptable salt thereof or a solvate thereof.

16. The pharmaceutical composition according to claim 15 which has a binding activity to a cannabinoid type 2 receptor.

17. The pharmaceutical composition according to claim 16 which has an agonistic activity to a cannabinoid type 2 receptor.

18. The pharmaceutical composition according to claim 16 which is useful as an anti-inflammatory agent.

19. The pharmaceutical composition according to claim 16 which is useful as an immunosuppressive agent.

20. The pharmaceutical composition according to claim 16 which is useful as a nephritis treating agent.

21. A method for treating inflammation which comprises administering the pharmaceutical composition according to claim 1.

22. A method of immunosuppression which comprises administering the pharmaceutical composition according to claim 1.

23. A method for treating nephritis which comprises administering the pharmaceutical composition according to claim 1.

24. Use of the compound according to claim 1 for manufacturing an anti-inflammatory agent.

25. Use of the compound according to claim 1 for manufacturing an immunosuppressive agent.

26. Use of the compound according to claim 1 for manufacturing a nephritis treating agent.

INTERNATIONAL SEARCH REPORT

International application No.
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A. CLASSIFICATION OF SUBJECT MATTER
Int.Cl' C07D277/18, 279/06, 279/08, 417/12, A61K31/426, 31/541, 31/5415, 31/547, A61P13/12, 29/00, 37/06, 43/00//(C07D417/12, C07D213:36, C07D279:06), (C07D417/12, C07D215:12, C07D279:06), (C07D417/12, C07D279:06, C07D333:34)
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED
Minimum documentation searched (classification system followed by classification symbols)
Int.Cl' C07D277/08-277/18,279/06-279/08,417/12,A61K31/426, 31/541-31/5415, 31/547, A61P13/12, 29/00, 37/00-37/06, 43/00

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
CAPLUS(STN), REGISTRY(STN), WPI(DIALOG), JICST(JOIS)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X A	GIELDANOWSKI, J., et al., "PHARMACOLOGICAL ACTIVITY IN THE GROUP OF NEW SUBSTITUTED THIAZOLOACETIC AND THIAZINOCAOROXYL ACID DERIVATIVES", Arch. Immunl. Ther. Exp., 26(1-6), pp.921-929 (1978)	1-6,24,25 7-20,26
X A	JP, 62-212378, A (Bayer Aktiengesellschaft), 18 September, 1987 (18.09.87), Claims; page 25, upper right column to page 26, upper left column; example & DE, 3632042, A & EP, 240680, A & US, 4771062, A	1-5,24 6-20,25,26
X A	JP, 2-3678, A (Janssen Pharmaceutica N.V.), 09 January, 1990 (09.01.90), Claims; page 14, upper left column to page 15, lower right column; example & EP, 331232, A & AU, 8930739, A & NO, 8900813, A & DK, 8900918, A & PT, 89875, A & FI, 8900931, A & CN, 1036569, A & ZA, 8901547, A & IL, 89426, A	1-5,24 6-20,25,26

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier document but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
27 November, 2000 (27.11.00)	12 December, 2000 (12.12.00)
Name and mailing address of the ISA/ Japanese Patent Office	Authorized officer
Facsimile No.	Telephone No.

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International application No.
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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	FR, 2201080, A (BADISCHE ANILIN- & SODA-FABRIK AG.), 26 April, 1974 (26.04.74),	1-5,24
A	Claims; page 4, line 1 to page 5, line 3 & DE, 2114097, A & GB, 1402103, A	6-20,25,26
X	JP, 2-223564, A (Ube Industries, Ltd.), 05 September, 1990 (05.09.90),	8-10,13
A	Claims; Table 1, & EP, 356158, A & ZA, 8906308, A & US, 5073558, A	11,12,14
X	JP, 63-41471, A (Nippon Soda Co., Ltd.), 22 February, 1988 (22.02.88),	8-10,13
A	Claims; Table 1 (Family: none)	11,12,14
X	JP, 57-134472, A (Hoechst Aktiengesellschaft), 19 August, 1982 (19.08.82),	1,2
A	Claims; page 9, lower right column to page 10, lower right column & EP, 55458, A & DE, 3049460, A & NO, 8104468, A & DK, 8105811, A & FI, 8104175, A & ZA, 8108968, A & US, 4421757, A & IL, 64653, A & ES, 8305342, A & ES, 8308549, A & ES, 8308550, A & ES, 8308551, A & ES, 8402829, A & CA, 1173836, A	3-20,24-26
X	JP, 59-172486, A (Janssen Pharmaceutica N.V.), 29 September, 1984 (29.09.84),	1,2
A	Claims; page 11, upper right column to lower left column; example & EP, 118138, A & AU, 8425097, A & NO, 8400735, A & NO, 8702221, A & NO, 9000396, A & DK, 8401070, A & DK, 9100783, A & DK, 9101088, A & FI, 8400781, A & PT, 78156, A & ZA, 8401449, A & US, 4619931, A & IL, 71066, A & CA, 1271194, A & JP, 5-246999, A & ES, 8505364, A & ES, 8506007, A & ES, 88507541, A	3-20,24-26
X	JP, 56-10180, A (Hoechst Aktiengesellschaft), 02 February, 1981 (02.02.81),	1,2
A	Claims; page 18, upper left column to page 19, upper left column; example & DE, 2926771, A & NO, 8001995, A & NO, 8404120, A & EP, 23964, A & DK, 8002865, A & FI, 8002094, A & ZA, 8003979, A & US, 4346088, A & CA, 1156240, A & IL, 60468, A & IL, 70114, A	3-20,24-26
X	JP, 52-51364, A (Hoechst Aktiengesellschaft), 25 April, 1977 (25.04.77),	1,2
A	Claims; example & BE, 847352, A & DE, 2546165, A & NL, 7611159, A & SE, 7611504, A & NO, 7603502, A & FI, 7602920, A & DK, 7604640, A & FR, 2327778, A & US, 4083979, A & AT, 7902625, A	3-20,24-26

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International application No.
PCT/JP00/06185

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	& AT, 7607655, A & GB, 1563323, A & CA, 1083581, A	
X	JP, 52-17468, A (Hoechst Aktiengesellschaft),	1,2
	09 February, 1977 (09.02.77),	
A	Claims; example	3-20,24-26
	& BE, 844666, A & DE, 2533821, A & NL, 7608206, A & SE, 7608545, A & NO, 7602625, A & DK, 7603404, A & FI, 7602140, A & FR, 2319345, A & US, 4061647, A & GB, 1522107, A & AT, 7605555, A & IL, 50146, A & CA, 1077492, A	
X	JP, 51-54555, A (Hoechst Aktiengesellschaft),	1,2,
	13 May, 1976 (13.05.76),	
A	Claims; page 28, lower right column to page 29, upper right column; example	3-20,24-36
	& JP, 52-83511, A & NL, 5708848, A & BE, 831794, A & IL, 47779, A & DE, 2436263, A & SE, 7508476, A & PT, 64112, A & NO, 7502636, A & DK, 750340, A & FI, 7502131, A & FR, 2282882, A & ZA, 7504772, A & DD, 121112, A & US, 4061761, A & US, 4125614, A & GB, 1513948, A & CA, 1054596, A & CH, 617431, A & CH, 623316, A & CH, 624677, A & CH, 624678, A & AT, 7505770, A & AT, 7707817, A & AT, 7707814, A & AT, 7707815, A & AT, 7707816, A	
X	JP, 50-37775, A (Egyt Gyogyszervegyeszeti Gyar),	1,2,
	08 April, 1975 (08.04.75),	
A	Claims; page 2; example	3-10,24-26
	& NL, 7409315, A & DE, 2433104, A & SE, 7409092, A & DK, 7403740, A & DD, 112452, A & FR, 2236495, A & CS, 7404954, A & GB, 1467385, A & AT, 7404954, A	
X	JP, 48-36169, A (Bayer Aktiengesellschaft),	1,2,
	28 May, 1973 (28.05.73),	
A	Claims; page 3, upper left column to page 4, upper right column; example	3-20,24,26
	& JP, 48-36168, A & BE, 788743, A & DE, 2145807, & RO, 68389, AA, & NL, 7212419, A & ZA, 7206271, A & FR, 2154512, A & DD, 103898, A & DD, 105990, A & GB, 1377265, A & RO, 84247, A & US, 3860590, A & AT, 7402318, A & AT, 7402319, A & SU, 455544, A & CH, 569724, A & CH, 587258, A & SU, 439988, A & SU, 505363, A & SU, 556728, A & RO, 84248, A & RO, 68372, A & IL, 40338, A & CA, 1007638, A	
X	JP, 48-23793, A (Imperial Chem. Ind. Ltd.),	1,2
	29 March, 1973 (29.03.73),	

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP00/06185

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	Claims; page 3, upper left column; example & DE, 2236970, A & BE, 786416, A & FR, 2147214, A & ZA, 7204731, A & SU, 847915, A & DD, 103645, A & GB, 1351031, A & US, 3845070, A & US,3925440,	3-20,24,26
X	US, 3678041, A (Etablissements Clin-Byla), 18 July, 1972 (18.07.72),	1,2
A	Claims; Column 1, lines 1 to 11; example & DE, 1770583, A & BE, 716140, A & AU, 6838776, A & ZA, 6703535, A & ZA, 6803535, A & CA, 897687, A & GB, 1224546, A & US, 3678041, A & US, 3704296, A & FR, 1604530, A	3-20,24,26
X	JP, 6-220053, A (Fuji Photo Film Co., Ltd.), 09 August, 1994 (09.08.94),	1,2
A	Claims; Par. Nos. [0014], [0015], [0024] & US, 5476945, A & US, 5618831, A	3-20,24,26
X	GAILWAD, N. J., et al., "Substituted-4-Thiazolidinones as Anticonvulsants", Indian J. Pharm. Sci., 46(5),	1,2
A	pp.170-171 (1984)	3-20,24,26
PX	WO, 00/42031, A2 (BAYER CORPORATION), 20 July, 2000 (20.07.00), Claims; example & AU, 200027087, A	1,2,8-10,13,15
A	JP, 11-80124, A (JAPAN TOBACCO INC.), 26 March, 1999 (26.03.99) & WO, 99/02499, A1 & AU, 9881279, A	1-20,24-26
A	MUNRO, S., et al., "Molecular characterization of a peripheral receptor of cannabinoids", NATURE, 365(2), pp.61-65 (1993)	1-20,24-26

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INTERNATIONAL SEARCH REPORT

International application No.
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Box I ***Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)***

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 21-23
because they relate to subject matter not required to be searched by this Authority, namely:

The inventions as set forth in claims 21 to 23 pertain to methods for treatment of the human body by therapy (Article 17(2)(a)(i) of the PCT and Rule 39.1(iv) of the Regulations under the PCT).

2. ☒ Claims Nos.: 1-20,24-26
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

(See extra sheet.)

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II **Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest
☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

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INTERNATIONAL SEARCH REPORT

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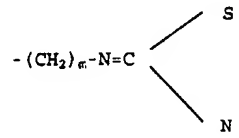
Continuation of Box No. I-2 of continuation of first sheet (1)

(The technical features of the inventions as set forth in claims 1 to 20 and claims 24 to 26 reside in the compounds per se represented by the formula (I) or (II) or utilization of these compounds as drugs. The compounds involved in the formulae (I) and (II) have nothing but the following chemical structure in common:



As stated in the documents, compounds having this chemical structure and medicinal compositions with the use of these compounds have been widely known. Therefore, the technical features cannot be considered as being sufficiently specified by the chemical structure. Moreover, only a part of compounds among compounds involved in a broad scope are supported in the description. Therefore, the claims and description fail to satisfy the definite requirements to such an extent as enabling meaningful international search.

In this report, therefore, the search has been practiced exclusively on compounds satisfying the following conditions by reference to the statement in the description:

- the substituent A is an optionally substituted phenyl or optionally substituted 3-pyridyl group;
- m is an integer of from 0 to 2;
- R^1 is an optionally substituted, linear C_{2-3} alkylene group; and
- R^2 is an alkyl, $-(C=R^5)-R^6$ or $-SO_2R^7$ group (wherein R^5, R^6 and R^7 are each as defined in claims).

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